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(54) Title: IDENTIFICATION OF TISSUE/CELL SPECIFIC MARKER GENES AND USE THEREOF

(57) Abstract: A cartilage array comprises a plurality of different polynucleotide probe spots stably associated with a solid surface of a carrier, whereby each of said spots is made of a unique polynucleotide that corresponds to one specific cartilage marker gene. Said specific cartilage marker genes preferably are at least in part selected from a group of 467 genes that could be shown to be cartilage related.

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**Identification of tissue/cell specific marker genes and  
use thereof**

**Cross References to Related Applications**

This application claims the priority of US provisional patent application 60/388994, filed June 14, 2002, the disclosure of which is incorporated herein by reference in its entirety.

**Field of the Invention**

The present invention relates to a method for the identification of tissue cell specific marker genes, a method for the determination of a disease state or developmental status of cells/tissue as well as to gene expression profiling of cartilage tissue. More specifically, the invention relates to microarrays containing a plurality of selected human chondrocyte specific sequences and their use for classification of cartilage donor tissue or generation of characteristic gene expression profiles of *in vitro* chondrocyte cultures. Such DNA arrays find use as a standard tool of molecular biology research and clinical diagnostics for all cartilaginous or related tissues.

**Background of the Invention**

**Limitation on current microarray technologies**

DNA array technology, also known as biochip or microarray technology, is currently revolutionizing modern biology. In this technology, a biological sample is applied to a glass slide or chip covered with an array of immobilized DNA probes. Sample nucleic acid complementary to specific probes on the array hybridizes and can be detected with high sensitivity with automated, computerized detectors. In this manner, hundreds to thousands of different individual hybridization experiments can be performed simultaneously. This allows assays of enormous complexity to be carried out – for example, an analysis of the entire gene expression

profile of a cancer cell – with simplicity unimaginable only a few years ago. As a consequence many patents as well as scientific publications have accumulated during the last years. U.S. 6,194,158 discloses characteristic genes and gene expression useful in screening for, diagnosis of, monitoring of, and therapeutic treatment of brain cancer. U.S. 6,218,122 discloses methods for determining or monitoring the progression of disease states or the efficacy of therapeutic regimens within human patients. U.S. 6'077'673 discloses mouse arrays having a plurality of probe polynucleotides corresponding to a key mouse gene for expression analysis of critical mouse genes. A list of representative scientific papers dealing with monitoring the expression level of a large number of transcripts within a cell at any time are as follows: Schena et al., 1995, Quantitative monitoring of gene expression patterns with a complementary DNA-microarray, *Science* 270: 467-470; Lockhart et al., 1996, Expression monitoring by hybridization to high-density oligonucleotide arrays, *Nature Biotechnology* 14:1675-1680; Blanchard et al., 1996, Sequence to array: Probing the genome's secrets, *Nature Biotechnology* 14:1649. Qi et al., 2003, Identification of genes responsible for osteoblast differentiation from human mesodermal progenitor cells *PNAS* 18;100(6):3305-10. While this list of scientific papers and patents reflects without any doubt the great potential of microarrays, there are a couple of yet unsolved problems that are more and more discussed among the scientific community. Especially, these problems are data overflow, representative sample collection, RNA processing and inappropriate data analysis. It is even suspected that within next five years, many of conclusions drawn from published data will be revised or refuted. Thus there remains a real and unmet need for advanced microarray solutions, targeted to specific tissues above all with respect to simplification and substantiation of the process of data generation and data handling. With respect to this issue the disclosed invention has made considerable contribution in the cartilage area with a cartilage-specific microarray containing a manageable number of cartilage relevant genes.



Limitation on the number of cartilage relevant genes

Until today the number of cartilage-relevant genes (genes that have been associated a potential functional role on cartilage biology, homeostasis or pathology) is very limited. Approximately, 100-200 genes have been described in the literature in any relationship to cartilage tissue. While existing publications e.g. Heller et al PNAS, 94; 2150-2155; 1997 have described analysis of inflammatory diseases of cartilage and Sekiya et al PNAS 99; 4397-4402; 2001 cartilage formation from stem cells with microarrays, a comprehensive analysis and determination of characteristic gene expression profiles for 2D, 3D, fetal, adult and pathological chondrocytes cell cultures cultivated under different conditions has not been performed up to now. While in patent WO01/24833 A2 a few markers have been determined that are associated with chondrocytes and their phenotype stability, it will not be possible to perform a detailed gene expression analysis and to define specific fingerprints. Therefore the possibility of characterizing culture conditions or cartilage tissue samples can not be thoroughly addressed.

Completion of the human genome first project draft on 2000 has revealed that the human genome comprises ~30000-35000 human genes. Estimates show that the number and type of active genes vary significantly between different tissues and may increase up to a couple of 10000 for complex tissues, e.g. brain. As a consequence, many genes albeit fully sequenced may have yet not been disclosed to be functionally up- or down regulated in cartilage or cartilage derived cells. The inventive approach described herein has made possible to up to now disclose a total of 467 known and additional genes being differentially expressed in a significant and objective manner within chondrocytes or chondrogenic cells.

By means of the already known and additionally found to be cartilage related genes, a strategy to best address and represent chondrocytes cultured under different conditions has been developed in the scope of the present invention.

### Summary of the Invention

In a first aspect the present invention relates to a method for the identification of tissue/cell specific marker genes comprising

5 a) taking tissue and/or cells of at least one developmental stage and/or at least one disease state, and/or

cultivating said tissue and/or cells *in vitro* under at least one culture condition,

b) determination of gene expression profiles of said tissue/cells and/or *in vitro* cultivated tissue/cells and

10 c) identification of specific marker genes by bioinformatic analysis of said gene expression profiles.

In particular, the first aspect relates to a method for the identification of tissue/cell specific marker genes comprising cultivating  
15 tissue/cells of different developmental stages and/or health conditions *in vitro* under different culture conditions, determination of gene expression profiles of said *in vitro* cultivated cartilage tissue and identification of specific marker genes by bioinformatic analysis of said gene expression profiles.

In a preferred embodiment said tissue is selected from the group consisting of fetal tissue, adolescent tissue, adult tissue, healthy  
20 tissue, pathological tissue, progenitor cells such as stem cells or cells derived from the same precursor lineage. Preferred culture conditions are 2D and 3D *in vitro* cultures and the gene expression profiles are preferably determined by means of a micro-array. The bioinformatic analysis of said gene expression profiles is preferably done by cluster software such as e.g.  
25 cluster analysis.

In a preferred embodiment said tissue is cartilage.

A second aspect of the present invention relates to a method for the determination of a disease state or developmental status of cells/tissue or the physiological potential of cells/tissue. Said method  
30 comprises establishing a profile of cellular constituents, preferably a gene expression profile, of said cells or tissue, comparison of said resulting gene expression profile with gene expression profiles characteristic for a particular status or physiological potential of the examined cells or tissue.

Said method can e.g. be. used to assess the redifferentiation potential of cells or tissue, the assessment of the quality of tissue biopsies for diagnostic and prognostic purposes regarding *in vitro* tissue engineering applications, the assessment of the quality of *in vitro* produced cells such as e.g. mesenchymal cells, stem cells or embryonic cells or of *in vitro* produced tissue for therapeutical applications and for determining the effect of one or more growth factors, media compositions or drugs on cells or tissue. Based on said method it is e.g. possible to set up different *in vitro* culture conditions for cells/tissue allowing the cultivation of cells/tissue which retain their potential for differentiation.

In a preferred embodiment said cells or tissue is cartilage tissue or chondrocytes and the array comprises polynucleotide probes of tissue specific marker genes.

In a further preferred embodiment said profile is a gene expression profile which is determined by means of a micro-array.

A further object of the present invention is a method for the determination of characteristic profiles for clinical use comprising correlating the patient data of the biopsy donor with the gene expression profile of said biopsy cells/tissue. Preferably said gene expression profile has been determined according to the above disclosed method. The resulting profiles of said method are suitable tools in the clinic allowing an evaluation of further treatments of a patient.

The present invention provides characteristic gene expression profiles experimentally determined by using cartilaginous tissues as from individual human donors of various ages (fetal, adolescent, adult) and health conditions (healthy and arthritic) or cells thereof cultivated under different *in vitro* culture conditions (2D and 3D *in vitro* cultures, time follow ups). From these different gene expression profiles a set of hitherto 467 markers has been deduced that can be used to design and produce a cartilage specific microarray for commercial applications in the field of R&D, such as culture media development, drug screening etc., but also for clinical applications.

Gene expression analysis performed with such microarrays and the corresponding analytical procedure thereof can be used to assess quality control of human donor cartilage, e.g. biopsy and therefore optimization of any downstream tissue engineering process, for diagnostic  
5 evaluation of the patient and its candidate treatment methods, to ensure a cost-optimized procedure, to investigate and assess all kind of 2D- and 3D *in vitro* cultures performed with human chondrocytes or chondrogenic cells, e.g. stem cells, to screen all kind of drugs, e.g. hormones, growth factors within the above mentioned *in vitro* cultures regarding a potential beneficial  
10 effect and quality assessment of *in vitro* produced tissue performed by tissue engineered procedures.

In a further aspect the present invention provides a cartilage array comprising a plurality of different polynucleotide probe spots stably  
associated with a solid surface of a carrier, whereby each of said spots is  
15 made of a unique polynucleotide that corresponds to one specific cartilage marker gene.

A preferred cartilage array of the present invention comprises at least two spots that have different nucleotide sequences but of the same cartilage marker gene, more preferably at least 10 spots indicative  
20 for one tissue or cell status, whereby said at least 10 spots can be selected from different sequences of one gene or from different genes or a combination thereof.

In a preferred embodiment said polynucleotides of the array do not cross hybridize under stringent conditions with each other.

25 In a preferred embodiment of the present invention the cartilage array comprises spots that are indicative for at least two tissue or cell status, preferably 3.

A further preferred inventive cartilage array is an array wherein at least part of the cartilage marker genes are selected from the 467  
30 genes listed in the description, preferably at least 10 %, more preferably at least 50 %, most preferably about 100 %.

A further preferred inventive cartilage array is an array wherein at least part of the cartilage marker genes are selected from a

subgroup of the 467 genes listed in the description, wherein said subgroup consists of the most tissue specific 200 genes.

In another preferred embodiment the status is selected from biopsies and/or 2D cultures and/or 3D cultures of healthy adult, healthy fetal/infant, undesired adult, undesired fetal/infant or progenitor cells like e.g. stem cells or cells derived from the same precursor lineage.

In a further preferred embodiment of the present invention the polynucleotide probes of the cartilage array have a length of at least 10 nucleotides, preferably at least 20 nucleotides. The probes can also have a length of 30 nucleotides, 50 nucleotides or 70 nucleotides. It is as well possible to use PCR derived products produced from cDNA clones.

In a preferred embodiment the carrier of the inventive cartilage array is attached to coated glass, nylon or any other material.

A further object of the present invention is a kit for use in a hybridization assay, wherein said kit comprises a cartilage array of the present invention. In a preferred embodiment said kit comprises reagents for generating a labelled target polynucleotide sample, a hybridization buffer and a wash medium.

#### **Description of the Figures**

The present invention will be further understood from the following description with reference to the tables and figures where:

Tab.I shows the determined number of all genes in the corresponding SOM analysis being differentially expressed according to microarray analyses of a variety of *in vitro* chondrocyte cultures according to predefined criteria. From these data sets specific expression profiles can be deduced that are characteristic for different cell culture conditions.

Tab.II shows the extracted and reviewed genes deduced from Tab I in order to have only single entry numbers. Since most of these genes have never been described in any relationship to cartilage, they can be considered as novel cartilage marker (positive/negative markers) or key cartilage genes.

Tab III shows a subset of marker genes from Tab. II that has been used for the production of a micro-array. Included is a subset from Tab II and genes known from the literature.

5 Tab IV shows the results of the analysis of the 467 cartilage specific marker genes.

Tab V shows the samples used in Examples 1, 2 and 3. Human chondrocytes isolated from 4 different donors were proliferated and kept in 3D-like pellet culture for 7 and 14 days resulting in a total number of 12 samples.

10 Fig.1 shows a classical result from an analysis performed with self-organizing-maps. This software clusters all genes together in sub clusters that show a similar expression profile. The number of marker genes for the corresponding analysis e.g. 2D vs. 3D cultures (see also Tab I) corresponds to the total number of genes in the sub clusters.

15 Fig 2 shows an example of a graphical presentation of a cluster analysis and viewed by the software treeview. This shows how cells from different origin and potential for *in vitro* cartilage formation are related to each other and allow a clearer classification of the cell sources. Fetal cells clearly produce different gene clusters compared to adult chondrocytes, 20 while failures are characterized by other gene clusters. Furthermore 3D cell cultures analyzed in a time dependent manner from different donors can be distinguished among each other and gene expression profiles will be grouped accordingly.

25 Fig 3: SOM analysis of all culture conditions and samples described in Example 2 and in Tab V.

Fig 4: SOM analysis for proliferated chondrocytes (t0) only, for the 4 donors. Gene expression pattern corresponding to donor 2 (the second spot from left hand side in every cluster) behaves different in most clusters.

30 Fig 5: SOM analysis of chondrocytes kept in 3D culture condition for 7 days (t7). Gene expression pattern from donor 3 (the third spot from left hand side in every cluster) is different for example in clusters c2 and c5.

Fig 6 shows self organized maps (SOM) of chondrocytes from same patients of Figures 4 and 5 kept under 3D culture condition for 14 days (t14).

Fig 7: cluster analysis of all culture conditions and samples described in Example 2 and in Tab V. This figure shows a subset of 88 hierarchical clustered genes (rows) and samples (columns) demonstrating similar gene expression behavior of chondrocytes under different culture conditions. For example proliferated cells (#1, #2, #4, #5, #7, #8, #10, #11) can easily be discriminated from cells kept in 3D-like pellet culture for 14 days (3#, 6#, 9#, 12#).

Fig 8: cluster analysis of human aortic fibroblasts vs. chondrocytes. This figure shows a subset of selected clusters of human aortic fibroblasts cells compared to human chondrocytes both kept in 3D pellet cultures for 14 days. The dendrogram in the upper part of the figure shows the ability of CART-CHIP™ 300 microarray described in this invention to discriminate between different cell lines.

Fig 9: cluster analysis of Interleukin-1 treated vs. untreated human chondrocytes. This figure demonstrates a subset of representative gene clusters allowing differentiation between cells treated with Interleukin-1 from untreated cells both kept in 3D pellet cultures as well as for proliferated cells.

### Detailed Description of the Invention

#### Definitions

*2D cultures* as used in the scope of the present invention are anchorage dependent chondrocyte cultures cultivated on plastic culture devices.

*3D cultures* as used in the scope of the present invention are chondrocytes cultured in a three dimensional environment, namely either a) scaffold-free, such as small high density pellet cultures ( $0.25 \cdot 10^6$  cells) or as high density cultures using  $50 \cdot 10^6$  cells/ml or aliquots thereof; or b) by using a synthetic scaffold such as PGA, PLA, or mixtures

thereof or biological substances such as agarose, alginate, chitosan or collagen.

5 *failures* as used in the scope of the present invention are chondrocytes cultured in a three dimensional environment that are not able to synthesize new extracellular matrix thereby compromising the production of new living tissue engineered cartilage equivalents.

*gene expression profile* as used in the scope of the present invention is a profile of genes that are up or down regulated according to different cell conditions.

10 *fingerprint* as used in the scope of the present invention refers to a gene expression profile characteristic for a cellular status.

*tissue or cell status* as used in the scope of the present invention refers to a tissue or cells thereof having a certain metabolic or activity status.

15 *new extracellular matrix* as used in the scope of the present invention designates living cartilage-like tissue.

*micro-array* as used in the scope of the present invention is used in its original scope that encompasses embodiments today sometimes refused to as "macro-arrays".

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### The Invention

The present invention provides cartilage-specific gene arrays as well as methods for their use. In the subject cartilage arrays, a plurality of polynucleotide probe spots are stably associated with the surface of a solid carrier, preferably a surface of a microscope glass slide. Each different polynucleotide probe spot is made of a unique polynucleotide that corresponds to a key cartilage gene of interest. Thus, the subject arrays find particular use in gene expression assays of key cartilage genes. In further describing the subject of the invention, the cartilage specific microarrays are first discussed, followed by a review of representative applications in which the subject arrays may be employed.

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### ***Arrays of the Subject Invention-General Description***

#### **Selection of novel key cartilage specific genes:**

A critical feature of the subject arrays is that all of the probe polynucleotide spots of the array correspond to human key cartilage genes that have been found through unique selection processes and criteria. As a result of said processes, up to now 467 different key human cartilage genes that are under tight transcriptional role have been discovered, some of them being not described before in any relationship to cartilage. In more detail, different microarray analyses were performed by using cartilaginous tissues as from individual human donors of various ages (fetal, adolescent, adult) and health conditions (healthy and arthritic) or cells thereof cultivated under different *in vitro* culture conditions (2D and 3D *in vitro* cultures, time follow ups). This variety of cartilage cell sources and different culture conditions was set up to grasp the highest possible number of genes differentially expressed and thus being indicative of a potential role.

It has been found that specific chondrocyte culture conditions are of great importance for the present invention that discloses a plurality of novel key cartilage genes as well as characteristic and meaningful gene expression patterns. For this reason, the strategy and criteria of the analysed *in vitro* human chondrocyte cultures are described in more detail. The principal experimental setup included both the cultivation of chondrocytes in an anchorage dependent condition, known as 2D cultures for expansion of cells e.g. where the passages is variable but at least more than one, as well as cultivation of chondrocytes in an anchorage independent condition, known as 3D cultures for (re-)differentiation and de novo tissue formation of cells. These are the key steps of any tissue engineering process where autologous tissue equivalents are produced. Since the cell source is either a small biopsy, a small bone marrow aspirate in case of mesenchymal stem cells or other tissue with a limited number of pre-chondrogenic cells, it is first necessary to isolate those cells in order to be able to multiply the cell number drastically. In case of a cartilage biopsy, cells are released from their surrounding extracellular matrix by collagenase digestion and then seeded onto the surface of plastic tissue culture flasks.

The proliferation may take place either in the presence or absence of fetal serum combined with conventional DMEM/F12 medium. Cells can then be passaged by trypsin treatment over several rounds. As a major drawback of this necessary cell expansion, the cells lose their differentiated phenotype and assume a de-differentiated phenotype with altered gene expression. It is further known that with increasing number of passages the state of de-differentiation also advances. As a consequence, genes being transcriptionally upregulated under such artificial culture conditions are cartilage relevant in a manner being indicative of an undesired cellular status. It is also quite common to designate these genes as de-differentiation or negative markers. While healthy tissue in general has been found to re-differentiate in 3D culture after up to 4 passages in 2D cultures, tissue of undesired cellular status cultivated under usual conditions, such as usual culture media, usually does not re-differentiate in 3D culture after at most 4 passages in 2D culture.

Subculture modulated chondrocytes that do not express differentiation markers reexpress the differentiated phenotype in response to the anchorage-independence resulting from various 3D culture models, e.g. high density cultures, agarose or alginate cultures, or cultures within synthetic scaffolds such as made of polyglycolic acid (PGA), polylactic acid (PLA) or mixtures thereof. To set up three dimensional cell cultures the cells are detached after proliferation by trypsin treatment and embedded either in gel-like substances such as alginate, seeded within a porous scaffold such as PGA or cultivated as high-density cultures, only. The time for the analysis may vary and ideally addresses several time points (up to several weeks). Thus 3D *in vitro* chondrocyte cultures support the differentiated phenotype of chondrocytes and can be used to discover cartilage relevant genes or differentiation markers. It should be noted however, that reversibility of the de-differentiation process is dependent on the number of passages and can become irreversible or at least partially irreversible at higher passage numbers (under usual conditions at most about 4 passages). As a rule the time course of de- and re-differentiation are similar. During skeletal development, cartilage serves as a template for

bone formation. Chondrocytes of fetal or infant (< 1 year) or growth plate cartilage pass through different stages and exhibit several distinct phenotypes, such as resting, proliferating, and hypertrophic chondrocytes. Progression through each of these phases is accompanied by profound changes in gene expression patterns. Further, evidence has accumulated that the successful sequence of cartilage repair via tissue engineering recapitulates aspects of embryonic tissue formation. For these reasons, it is important to consider fetal and infant cartilaginous tissue. Cells isolated from human fetal/infant cartilage that are cultivated in 2D and 3D culture systems as described above are especially helpful to understand the mechanisms underlying the phenotypic instability of chondrocytes and the related gene expression patterns. These 2D and 3D culture system may then be analyzed to deduce gene expression profiles and to define marker genes that are characteristic for the (re-)differentiation process. Thus maintenance of chondrocyte-specific phenotype being crucial for normal structure and biomechanical properties of articular cartilage may be better understood and have important implications for modern therapeutic biological applications.

The above mentioned experimental setup for 2D and 3D cultures may be even expanded to compare human adult cells with human fetal/infant chondrocytic cells of age <1 year. The comparison of gene expression profiles of adult versus fetal/infant human chondrocytes during the *in vitro* cartilage formation process is an important aspect since marker genes associated with developmental aspects are revealed. This can be of further interest when 3D cell cultures need to be optimized for their *in vitro* performance for the production of new tissue by e.g. adding growth factors that are found to play a major role during the early onset of cartilage formation *in vivo*.

Another experimental setup found in the scope of this invention includes the *in vitro* culture of cells harvested from cartilaginous areas of arthritic knee joints. Osteoarthritis (OA) results from the failure of chondrocytes within the joint to maintain the balance between synthesis and degradation of extracellular matrix. OA is a multifactorial disorder in

which aging, genetic, hormonal and mechanical factors are all major contributors to its onset and progression. With progressing disease state, the articular chondrocytes ability to maintain homeostasis and functionality is increasingly disappearing. As a consequence, the phenotype of osteoarthritic chondrocytes compared with normal chondrocytes exhibits remarkable changes. Gene expression profiling allows characterization of the osteoarthritic cellular phenotype, a key determinant for understanding and manipulation of osteoarthritic processes. By studying and comparing the gene expression profiles of chondrocytes harvested from pathological and healthy human cartilage areas it becomes possible to identify marker genes that are able to predict the future outcome of cell cultures used for *in vitro* tissue engineering applications. This also relates to the very critical question of the assessment of the quality of the starting biopsy material that is being used for downstream applications like tissue engineering. By having this important information before performing any downstream applications like e.g. proliferation and consecutive 3D *in vitro* tissue formation, the further steps of any process can then be adapted or even not performed at all because of inadequate quality of biopsy material. Such decision may be of high relevance when tissue-engineering processes are transferred or applied in the clinic. Gene expression profiling of chondrocytes may then be used as a diagnostic tool to allow and to choose that therapeutic approach with the most promising clinical outcome.

A further important aspect of the invention is the observation that chondrocytes derived from osteoarthritic patient material always qualify for anchorage dependent proliferation in 2D over several passages. These cells however, if subsequently induced to re-differentiate by culturing them as 3D high density pellets, do not survive over an extended time period, in most cases they die in culture by undergoing apoptosis. It is assumed that these cells, due to an altered phenotype, are not capable of producing the critical survival factors in the appropriate concentrations, above all extracellular matrix components providing intercellular spaces as they occur in native cartilage. Cells that are not suitable to be cultured within 3D high density cultures are herein referred to

as „failures“. These impaired cell cultures can be used to set up representative “failure” systems, where cells from different pathological cartilage sources are harvested, proliferated and cultivated in 3D high density pellet culture systems. After each of these experimental steps, RNA  
5 can be isolated from the different cell sources and combined to create “failure pools”. These failure pools are very well suitable to identify general marker genes being indicative of the onset of osteoarthritis.

For finding cartilage relevant genes, and for determining their presence dependent on the specific cartilage type such as age, health  
10 etc., sufficient material must be generated, e.g. by 2D culturing over several passages, and optionally 3D culturing. Said material then can on be subjected to usual gene analyses, and the tissue specific genes determined. Cartilage samples are classified prior to culturing and/or after culturing to get the information needed for later interpretation of the gene  
15 expression profile.

A further experimental setup of the current inventions discloses the analysis of chondrocytes grown in 3D cultures isolated from pathological human cartilage and analyzed in a time dependent manner. This experimental set-up allows to study the apoptotic process and to  
20 further define additional dynamic and characteristic gene expression profiles, useful for deducing and further assessment of the quality of the biopsy material.

The microarray process and strategy for disclosing all the cartilage relevant genes with the above-mentioned tissues and cell culture  
25 criteria will be described in the following. An important issue of the inovative strategy used by the inventors of the present inventions is to use various microarrays containing a high number of genes comprising different functional categories preferentially by representing the whole genome. The broader the microarray regarding the coverage of the human genome the  
30 more genes associated with chondrocyte cell cultures can be determined. The chosen strategy of the inventors was not obvious to a person skilled in the art.

RNA isolated from the above mentioned different cell cultures conditions may be radioactive labeled with e.g.  $^{33}\text{P}$  or fluorescence like e.g. Cy3 and hybridized to the corresponding filters or microarrays. After hybridization each array may then be scanned and the corresponding signals measured (Tab IV). This raw data file needs then to be calibrated and normalized in a manner to create an input file for the further downstream analysis process. In principle if the data are normalized an expression profile is created. To identify the key cartilage marker genes being differentially expressed under the chosen criteria, tedious bioinformatic analysis are conducted. Corresponding cell cultures and their expression profiles are therefore compared and analyzed accordingly and the different clusters of marker genes determined by software analysis e.g. self-organizing maps (herein referred to as SOM). A representative example of a result for the comparison of different gene expression profiles from different cell culture conditions performed by SOM analysis is given in Fig.1. By performing SOM analysis genes that are similarly expressed are clustered together in so-called sub clusters. The total amount of marker genes for one analysis corresponds to the total amount of sub clusters containing the corresponding genes. Table I in the appendix summarize the results of all the different analysis performed and encompasses all the genes determined for every set of cell culture analysis.

By performing this analytical procedure the analysis reveals several characteristic up and down regulated marker genes for different cellular culture conditions. From these marker genes characteristic expression profiles can then be deduced and used as a benchmark for the comparison or further characterization of other cell cultures.

Hence, on the one hand previously unknown cartilage-relevant genes associated with different culture conditions and on the other hand characteristic gene expression profiles (cellular fingerprints) indicative of a stage of development, a disease state or a particular selected cell culture condition are revealed. These fingerprints are part of the current invention and are of major importance for the classification and

characterization of chondrocytes cultivated under different culture conditions.

Since the gene clusters from all the different analysis contain repetitive gene entries, they have been further processed so that only single entry genes are recorded (see Tab II). This 467 selected sequences are thus all key cartilage genes that are activated and thus differentially expressed according to a stage of development, a disease state or a particular selected cell culture condition and are part of the current invention. A list of all 467 genes with their Pubmed accession no. and a description is given below See also Tables II and III):

## List of Table II related sequences:

Pubmed Accession No	Description
AA283693	Human osteoclast stimulating factor mRNA, complete cds
AA845156	Serine protease inhibitor, Kazal type 1
R52548	Human superoxide dismutase (SOD-1) mRNA, complete cds
T67128	ARYLAMINE N-ACETYLTRANSFERASE, MONOMORPHIC
AA845015	Elastase 1, pancreatic (elastase IIA)
AA937895	Antigen identified by monoclonal antibodies 12E7, F21 and O13
AA844998	Pancreatic polypeptide
AA844818	Amylase, alpha 2A; pancreatic
AA894557	Creatine kinase B
AA872001	Annexin VI (p68)
H09590	Human mRNA for eukaryotic initiation factor 4A1
AA868278	Testis specific protein 1 (probe H4-1 p3-1)
AA490855	Acid finger protein ZNF173
H05820	Human MRL3 mRNA for ribosomal protein L3 homologue ( MRL3 = mammalian ribosome L3 )
N57766	Agammaglobulinaemia protein-tyrosine kinase atk
AA873885	Alkaline phosphatase, liver/bone/kidney
AA878880	Interferon (gamma)-induced cell line; protein 10 from
R54818	Human eukaryotic initiation factor 2B-epsilon mRNA, partial cds
AA458630	RENIN PRECURSOR, RENAL
W37864	Phosphatase and tensin homolog (mutated in multiple advanced cancers 1)
N63192	Phenylethanolamine N-methyltransferase
R55789	Human X11 protein mRNA, partial cds
R56871	Human chromatin assembly factor-I p60 subunit mRNA, complete cds
AA448659	M-PHASE INDUCER PHOSPHATASE 2
AA235388	Tropomodulin
W37769	Chromogranin B (secretogranin 1)
AA421701	H.sapiens mRNA for MUF1 protein
N81029	Collagen, type XVIII, alpha 1
AA644128	Nuclear autoantigenic sperm protein (histone-binding)
N26536	ATPase, Cu++ transporting, beta polypeptide (Wilson disease)
AA890663	Human protein kinase PAK1 mRNA, complete cds
AA405987	Glycerol kinase 2 (testis specific)
AA888182	Ribosomal protein S4, X-linked
H09730	Adenylate kinase 2 (adk2)
AA285155	CDC46 HOMOLOG
AA873351	Ribosomal protein L35a
H12320	CAMP-RESPONSE ELEMENT BINDING PROTEIN
AA856556	Ribosomal protein S28
R43581	Human guanine nucleotide-binding protein G-s, alpha subunit mRNA, partial cds
AA633768	60S RIBOSOMAL PROTEIN L24
AA496880	Ribosomal protein L5
AA625632	Ubiquitin A-52 residue ribosomal protein fusion product 1
R40850	H.sapiens mRNA for alpha-centractin
AA486072	Small inducible cytokine A5 (RANTES)
N80129	Metallothionein 1L
T67270	UBIQUINOL-CYTOCHROME C REDUCTASE COMPLEX SUBUNIT VI REQUIRING PROTEIN
AA775364	60S RIBOSOMAL PROTEIN L30
AA464743	Ribosomal protein L21
AA663983	Triosephosphate isomerase 1
AA634008	40S RIBOSOMAL PROTEIN S23



AA683050 40S RIBOSOMAL PROTEIN S8  
AA775874 60S RIBOSOMAL PROTEIN L18  
AA029934 Integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)  
AA872397 GALECTIN-2  
AA428195 Protein tyrosine phosphatase, non-receptor type 2  
AA478724 Insulin-like growth factor binding protein 6  
T40541 H.sapiens mRNA for human giant larvae homolog  
N33214 H.sapiens mRNA for membrane-type matrix metalloproteinase 1  
W69399 Homo sapiens adenosine triphosphatase mRNA, complete cds  
H85454 Homo sapiens delayed-rectifier K<sup>+</sup> channel alpha subunit (KCNS1) mRNA, complete cds  
T71284 Complement component 1, q subcomponent, beta polypeptide  
N95418 Human FK-506 binding protein homologue (FKBP38) mRNA, complete cds  
AA430675 Human DNA repair protein XRCC9 (XRCC9) mRNA, complete cds  
AA682851 Homo sapiens mRNA for ERp28 protein  
AA427433 PROTEIN PHOSPHATASE PP2A, 65 KD REGULATORY SUBUNIT, ALPHA ISOFORM  
AA100296 H.sapiens PAP mRNA  
AA070997 Proteasome (prosome, macropain) subunit, beta type, 6  
R27585 Proteasome component C2  
N71628 Spi-B transcription factor (Spi-1/PU.1 related)  
AA464566 Human mRNA for LDL-receptor related protein  
AA043228 Calponin 3, acidic  
AA478273 APEX nuclease (multifunctional DNA repair enzyme)  
H05619 Homo sapiens GDNF family receptor alpha 2 (GFRalpha2) mRNA, complete cds  
AA405562 Protein phosphatase 4 (formerly X), catalytic subunit  
AA147043 Homo sapiens CAGH1a (CAGH1) mRNA, partial cds  
AA035384 Homo sapiens mRNA for small subunit of cytochrome b in succinate dehydrogenase complex, complete cds  
R60150 Human mRNA for histidyl-tRNA synthetase (HRS)  
N64051 Homo sapiens Werner syndrome gene, complete cds  
AA405748 SPLICING FACTOR U2AF 65 KD SUBUNIT  
AA461110 Homo sapiens growth-arrest-specific protein (gas) mRNA, complete cds  
AA845167 ELASTASE IIIA PRECURSOR  
AA443118 Homo sapiens mRNA for CD151, complete cds  
N92319 Glycoprotein Ib (platelet), beta polypeptide  
AA187148 Core-binding factor, beta subunit  
AA253413 Friedreich ataxia  
AA046701 ATP SYNTHASE LIPID-BINDING PROTEIN P1 PRECURSOR  
AA164562 Homo sapiens actin-related protein Arp3 (ARP3) mRNA, complete cds  
AA496357 Homo sapiens SKB1Hs mRNA, complete cds  
AA180742 TUBULIN ALPHA-4 CHAIN  
AA454743 Human protease M mRNA, complete cds  
AA437226 Interleukin 10 receptor  
AA458849 Homo sapiens placental bikunin mRNA, complete cds  
AA504891 Crystallin, alpha B  
AA609655 Homo sapiens mRNA for SCP-1, complete cds  
AA599158 MULTIFUNCTIONAL AMINOACYL-TRNA SYNTHETASE  
AA052932 Homo sapiens casein kinase I gamma 2 mRNA, complete cds  
AA789328 Homo Sapiens (clone PK2J) CDC2-related protein kinase (PISSLRE) mRNA, complete cds  
AA129537 Human GAP SH3 binding protein mRNA, complete cds  
AA486209 Low density lipoprotein-related protein-associated protein 1 (alpha-2-macroglobulin receptor-associated protein 1  
H39018 H.sapiens Syt V gene (genomic and cDNA sequence)  
AA464217 V-akt murine thymoma viral oncogene homolog 1

T95053	Homo sapiens Rigui (RIGUI) mRNA, complete cds
AA454646	LYMPHOTOXIN-BETA RECEPTOR PRECURSOR
AA448400	Human plectin (PLEC1) mRNA, complete cds
H13691	Major histocompatibility complex, class II, DM beta
AA132086	Homo sapiens RCL (Rcl) mRNA, complete cds
AA488073	Mucin 1, transmembrane
N40945	H.sapiens mRNA for DRES9 protein
R55705	Homo sapiens orexin receptor-1 mRNA, complete cds
H50114	Homo sapiens NMDA receptor mRNA, complete cds
AA452841	Human K-Cl cotransporter (hKCC1) mRNA, complete cds
W73790	IMMUNOGLOBULIN-RELATED 14.1 PROTEIN PRECURSOR
N30302	POSSIBLE GTP-BINDING PROTEIN HSR1
AA291556	Human ras inhibitor mRNA, 3' end
AA598510	Human APRT gene for adenine phosphoribosyltransferase
AA453787	Human TFIIIB related factor hBRF (HBRF) mRNA, complete cds
H05655	Human transcriptional activator mRNA, complete cds
AA419177	INTEGRAL MEMBRANE PROTEIN E16
AA458807	Human retinal protein (HRG4) mRNA, complete cds
AA293218	Cleavage stimulation factor, 3' pre-RNA, subunit 2, 64kD
W44860	Human calmodulin mRNA, complete cds
AA629862	Homo sapiens mRNA for smallest subunit of ubiquinol-cytochrome c reductase, complete cds
AA447674	Homo sapiens HIV-Nef associated acyl CoA thioesterase (hNAACTE) mRNA, complete cds
T52484	Nerve growth factor beta
AA496810	Protein kinase C substrate 80K-H
AA486233	G1 to S phase transition 1
AA079775	TYROSINE-PROTEIN KINASE CSK
W73889	Tetranectin (plasminogen-binding protein)
R50337	Solute carrier family 19 (folate transporter), member 1
R55046	MpV17 transgene, murine homolog, glomerulosclerosis
R46821	T-COMPLEX PROTEIN 1, ALPHA SUBUNIT
R87763	Human telencephalin precursor mRNA, complete cds
H69583	Human BTG2 (BTG2) mRNA, complete cds
R56046	Guanine nucleotide binding protein (G protein), alpha z polypeptide
AA922705	Glycogen phosphorylase B (brain form)
AA487571	Surfactant, pulmonary-associated protein C
AA402440	Homo sapiens exportin t mRNA, complete cds
H29521	ATP-binding cassette 3
AA490911	Homo sapiens drp1 mRNA, complete cds
AA486082	Homo sapiens sgk gene
AA678065	2,3-bisphosphoglycerate mutase
R43509	Human Gu binding protein mRNA, partial cds
N57553	Adenosine receptor A2
AA676955	Aplysia ras-related homolog 12
R14692	Human Na/H antiporter (APNH1) mRNA, complete cds
AA488979	Homo sapiens nucleolar protein (MSP58) mRNA, complete cds
AA443630	Aldehyde dehydrogenase 8
AA027840	H.sapiens mRNA for RIT protein
AA456830	Diacylglycerol kinase, alpha (80kD)
AA453015	H.sapiens L23-related mRNA
AA074446	Human GTP cyclohydrolase I feedback regulatory protein gene, complete cds
AA027042	DNA-DIRECTED RNA POLYMERASE II 23 KD POLYPEPTIDE
AA629923	Human mRNA for pM5 protein
AA460830	Homo sapiens (clone mf.18) RNA polymerase II mRNA, complete cds

AA454218 Homo sapiens transcription factor SL1 mRNA, complete cds  
AA046523 H.sapiens mRNA for centrin gene  
R51346 Human eIF-2-associated p67 homolog mRNA, complete cds  
AA029964 Human ataxin-2 related protein mRNA, partial cds  
AA489219 DUTP pyrophosphatase  
AA043133 Solute carrier family 16 (monocarboxylic acid transporters), member 1  
AA812973 Human mRNA for testis-specific TCP20, complete cds  
AA453471 GANGLIOSIDE GM2 ACTIVATOR PRECURSOR  
AA284693 Transcription factor AP-4 (activating enhancer-binding protein 4)  
N90281 Human B7 mRNA, complete cds  
AA629542 Brush-1  
AA679345 Human BTK region clone ftp-3 mRNA  
H37774 Tuberin  
T97181 Platelet factor 4  
AA454879 Plasminogen activator, urokinase receptor  
AA147640 Phosphorylase, glycogen; liver (Hers disease, glycogen storage disease type VI)  
AA757429 Human serotonin N-acetyltransferase mRNA, complete cds  
AA490991 Homo sapiens HnRNP F protein mRNA, complete cds  
AA422058 H.sapiens mRNA for D1075-like gene  
N66208 Human (ard-1) mRNA, complete cds  
AA630776 Human AP-3 complex delta subunit mRNA, complete cds  
AA827287 Human interferon-induced leucine zipper protein (IFP35) mRNA, partial cds  
AA488084 Superoxide dismutase 2, mitochondrial  
R89715 Protein kinase C, gamma  
AA490501 H.sapiens mRNA; UV Radiation Resistance Associated Gene  
N32199 Human melanoma antigen recognized by T-cells (MART-1) mRNA  
AA434404 DNA primase polypeptide 2A (58kD)  
N93686 Aldehyde dehydrogenase 7  
AA292676 Human metargidin precursor mRNA, complete cds  
AA464417 INTERFERON-INDUCIBLE PROTEIN 1-8U  
AA442092 Catenin (cadherin-associated protein), beta 1 (88kD)  
AA026644 Transcription factor 3 (E2A immunoglobulin enhancer binding factors E12/E47)  
AA481464 Peptidylprolyl isomerase B (cyclophilin B)  
T68859 Alpha-2-plasmin inhibitor (alpha-2-PI)  
AA699560 Surfeit 1  
AA705069 Human mRNA for receptor of retinoic acid  
AA457739 Homo sapiens putative OSP like protein mRNA, partial cds  
H99843 Homo sapiens mRNA for quinolinate phosphoribosyl transferase, complete cds  
AA399410 Signal transducer and activator of transcription 3 (acute-phase response factor)  
AA443039 HEAT SHOCK 70 KD PROTEIN 1  
AA164440 Human autoantigen pericentriol material 1 (PCM-1) mRNA, complete cds  
AA446453 Human mRNA for c-myc binding protein, complete cds  
AA280692 Diacylglycerol kinase delta  
AA031514 Matrix metalloproteinase 7 (matrilysin, uterine)  
R33154 Msh (Drosophila) homeo box homolog 1 (formerly homeo box 7)  
AA487452 Human DNA fragmentation factor-45 mRNA, complete cds  
AA400329 Human gene for neurofilament subunit M (NF-M)  
AA454668 Prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)  
AA486393 Cytokine receptor family II, member 4  
R52541 unknown EST  
AA171613 Homo sapiens carbonic anhydrase precursor (CA 12) mRNA, complete cds  
AA235706 Human TATA-binding protein associated factor 30 kDa subunit (tafil30) mRNA, complete cds  
AA668527 Human mucosal addressin cell adhesion molecule-1 (MAdCAM-1) mRNA, complete

	cds
T54144	Homo sapiens homolog of the Aspergillus nidulans sudD gene product mRNA, complete cds
R14080	Calcium modulating ligand
AA609599	Homo sapiens SSX3 (SSX3) mRNA, complete cds
AA489201	H.sapiens mRNA for PHAPI2b protein
R08876	Human 26S proteasome-associated pad1 homolog (POH1) mRNA, complete cds
H46425	H.sapiens Pur (pur-alpha) mRNA, complete cds
R56149	Human putative transmembrane protein (nma) mRNA, complete cds
AA454619	Homo sapiens mRNA for Hic-5, partial cds
H15445	H.sapiens mRNA for SEX gene
AA705225	Myosin, light polypeptide 4, alkali; atrial, embryonic
AA191488	Human high-affinity copper uptake protein (hCTR1) mRNA, complete cds
N64862	Human SLP-76 associated protein mRNA, complete cds
R45413	Human transmembrane 4 superfamily protein (SAS) mRNA, complete cds
R77293	Intercellular adhesion molecule 1 (CD54), human rhinovirus receptor
AA436187	Integrin, alpha M (complement component receptor 3, alpha; also known as CD11b (p170), macrophage antigen alpha polypeptide)
AA676470	H.sapiens IAI.3B mRNA
AA443634	Homo sapiens ubiquitin conjugating enzyme G2 (UBE2G2) mRNA, complete cds
AA664180	Glutathione peroxidase 3 (plasma)
W58658	H.sapiens mRNA for CLPP
H54023	Homo sapiens monocyte/macrophage Ig-related receptor MIR-10 (MIR cl-10) mRNA, complete cds
H73724	Cyclin-dependent kinase 6
T70031	Human neutral amino acid transporter B mRNA, complete cds
AA481758	DNAJ PROTEIN HOMOLOG 1
AA521431	Human profilin mRNA, complete cds
AA446103	ERGIC-53 PROTEIN PRECURSOR
N92646	Immunoglobulin gamma 3 (Gm marker)
AA453789	Protein-tyrosine kinase 7
AA425299	Homo sapiens ezrin-radixin-moesin binding phosphoprotein-50 mRNA, complete cds
AA868929	Troponin T1, skeletal, slow
R60019	Homolog 2 of Drosophila large discs
AA857343	Human putative RNA binding protein (RBP56) mRNA, complete cds
AA481438	Complement component 1 inhibitor (angioedema, hereditary)
AA399674	Human small proline rich protein (spr11) mRNA, clone 1292
T98887	Glucose-6-phosphatase
AA676404	Peptidylprolyl isomerase C (cyclophilin C)
H15747	Human HU-K4 mRNA, complete cds
H16958	Human glyceraldehyde 3-phosphate dehydrogenase mRNA
AA936783	Eukaryotic translation initiation factor 3 (eIF-3) p36 subunit
AA884709	Cytochrome P450 11 beta
H24688	Human SWI/SNF complex 170 KDa subunit (BAF170) mRNA, complete cds
AA884403	Human cardiotrophin-1 (CTF1) mRNA, complete cds
AA404619	5' nucleotidase (CD73)
AA598611	IMMEDIATE-EARLY RESPONSE PROTEIN NOT
H72875	GATA-binding protein 3
H63361	Eukaryotic translation initiation factor 2B (eIF-2B) alpha subunit
R39221	Human MAP kinase mRNA, complete cds
R02346	U1 snRNP 70K protein
R51835	unknown EST
R33031	H.sapiens mRNA for sigma 3B protein
AA412053	CD9 antigen
AA001897	Erythroid alpha-spectrin

W81191 Homo sapiens nucleolar autoantigen No55 mRNA, complete cds  
AA430552 Homo sapiens proline-rich Gla protein 2 (PRGP2) mRNA, complete cds  
AA394130 Human transducin-like protein mRNA, complete cds  
N92864 Human cleavage and polyadenylation specificity factor mRNA, complete cds  
AA457123 VALYL-TRNA SYNTHETASE  
R43320 Human guanine nucleotide-binding regulatory protein (Go-alpha) gene  
AA670430 Glutamate receptor, metabotropic 3  
H65066 Visinin-like 1  
AA458785 GUANYLATE CYCLASE SOLUBLE, BETA-1 CHAIN  
AA485871 H.sapiens mRNA for myosin-I beta  
T39411 Human 53K isoform of Type II phosphatidylinositol-4-phosphate 5-kinase (PIPK) mRNA, complete cds  
R00855 Homo sapiens 59 protein mRNA, 3' end  
H98666 Metallopeptidase 1 (33 kD)  
H72028 GELSOLIN PRECURSOR, PLASMA  
AA679177 Human follistatin-related protein precursor mRNA, complete cds  
N21576 Human mitochondrial 1,25-dihydroxyvitamin D3 24-hydroxylase mRNA, complete cds  
AA007419 Human RGP4 mRNA, complete cds  
T49657 Homo sapiens TWIK-related acid-sensitive K<sup>+</sup> channel (TASK) mRNA, complete cds  
N38959 Homo sapiens chaperonin containing t-complex polypeptide 1, beta subunit (Cctb) mRNA, complete cds  
R51912 Human somatostatin I gene and flanks  
H90415 Breast cancer 1, early onset  
H41489 Adaptin, beta 1 (beta prime)  
H15456 CALPAIN 1, LARGE  
W45415 ELASTASE IIIB PRECURSOR  
AA447751 Tyrosine hydroxylase  
AA487486 Cyclin D1 (PRAD1; parathyroid adenomatosis 1)  
R56604 Cholinergic receptor, nicotinic, alpha polypeptide 4  
T65772 pulmonary surfactant protein (SP5)  
H15085 ADP-ribosylation factor 4-like  
R61295 Human ADP/ATP translocase mRNA, 3' end, clone pHAT8  
T61256 H.sapiens KHK mRNA for ketohexokinase, clone pHKHK3a  
AA405731 Phosphoenolpyruvate carboxykinase 1 (soluble)  
T71879 Complement component C2  
R59927 Human mRNA for cytochrome c oxidase subunit VIc  
AA496780 Human small GTP binding protein Rab7 mRNA, complete cds  
AA176688 Human mRNA for lysosomal sialoglycoprotein, complete cds  
AA436163 Homo sapiens Pig12 (PIG12) mRNA, complete cds  
AA428778 Human placenta LERK-2 (EPLG2) mRNA, complete cds  
AA463225 Bone morphogenetic protein 4  
AA485426 Interferon (alpha, beta and omega) receptor 2  
W47485 Human sigma receptor mRNA, complete cds  
H84982 Human checkpoint suppressor 1 mRNA, complete cds  
AA504615 Homo sapiens mRNA for CAB1, complete cds  
H94487 Cathepsin E  
AA448959 Homo sapiens NADH:ubiquinone oxidoreductase 15 kDa IP subunit mRNA, nuclear gene encoding mitochondrial protein, complete cds  
AA070358 Transketolase (Wernicke-Korsakoff syndrome)  
AA453401 Human PH-20 homolog (LUCA2) mRNA, partial cds  
N66737 Collagen, type II, alpha 1 (primary osteoarthritis, spondyloepiphyseal dysplasia, congenital)  
AA666180 Human v-erbA related ear-2 gene  
AA857131 Human Tat-SF1 mRNA, complete cds  
AA479102 Protein kinase C, beta 1

AA456077	Homo sapiens mRNA for p27, complete cds
R87497	H.sapiens mRNA for 2.19 gene
AA718910	Human tax1-binding protein TXBP181 mRNA, complete cds
AA406269	Nuclear factor I/X (CCAAT-binding transcription factor)
N74623	Insulin-like growth factor 2 (somatomedin A)
H99364	Human chloride channel protein (CLCN7) mRNA, partial cds
AA447684	Small proline-rich protein 1B (cornifin)
AA282301	Homo sapiens nuclear dual-specificity phosphatase (SBF1) mRNA, partial cds
H99588	Human lymphoid nuclear protein (LAF-4) mRNA, complete cds
N53512	Homo sapiens alpha 2 delta calcium channel subunit isoform I mRNA, complete cds
AA683321	Homo sapiens PAR-5 mRNA, probable 5' end
AA608557	Damage-specific DNA binding protein 1 (127 kD)
AA757764	Homo sapiens mRNA for DNA-binding protein, complete cds
AA406064	Homo sapiens testis-specific Basic Protein Y 1 (BPY1) mRNA, complete cds
N54596	Human Krueppel-related zinc finger protein (H-plk) mRNA, complete cds
AA481988	Transcription factor 7 (T-cell specific)
N62394	Gap junction protein, beta 1, 32kD (connexin 32, Charcot-Marie-Tooth neuropathy, X-linked)
N26148	Zinc finger protein 148 (pHZ-52)
AA496678	B-cell CLL/lymphoma 3
AA400973	NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN PRECURSOR
AA497027	Human mRNA, clone HH109 (screened by the monoclonal antibody of insulin receptor substrate-1 (IRS-1))
N64508	Homo sapiens podocalyxin-like protein mRNA, complete cds
AA033564	H.sapiens mRNA for DGCR6 protein
AA446108	Endoglin (Osler-Rendu-Weber syndrome 1)
AA159577	Mucin 5, subtype B, tracheobronchial
R36958	unknown EST
AA629808	Ribosomal protein L6
AA482067	Human tazarotene-induced gene 2 (TIG2) mRNA, complete cds
AA669314	ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, delta subunit
AA775241	Aldolase A
R73584	Homo sapiens hydroxysteroid sulfotransferase SULT2B1a (HSST2) mRNA, complete cds
H28984	PHOSPHATIDYLSERINE SYNTHASE I
R44202	Homo sapiens catechol-O-methyltransferase (COMT) mRNA, complete cds
W70051	H.sapiens mRNA for M-phase phosphoprotein, mpp9
AA401972	Human RalGDS-like 2 (RGL2) mRNA, partial cds
AA236164	CATHEPSIN S PRECURSOR
R22412	Platelet/endothelial cell adhesion molecule (CD31 antigen)
AA424804	MULTIDRUG RESISTANCE-ASSOCIATED PROTEIN 1
AA669443	Eukaryotic translation initiation factor 5 (eIF5)
N69689	RAS-RELATED PROTEIN RAB-1A
H24316	AQUAPORIN-CHIP
AA074224	Recoverin
R36571	Human U1 snRNP-specific protein A gene
AA056465	Human 54 kDa protein mRNA, complete cds
AA633811	H.sapiens E4BP4 gene
AA457155	Human zinc-finger protein C2H2-150 mRNA, complete cds
AA459104	60S RIBOSOMAL PROTEIN L13
R40212	Human coatomer protein (HEPCOP) mRNA, complete cds
AA086476	Adenosine monophosphate deaminase 1 (isoform M)
AA663310	Thymidylate synthase
AA455640	Homo sapiens signalosome subunit 3 (Sgn3) mRNA, complete cds
AA496879	Human (clone E5.1) RNA-binding protein mRNA, complete cds

AA085749	Homo sapiens mRNA for ATP binding protein, complete cds
AA425755	Homo sapiens mRNA for leukemia associated gene 1
N52350	H.sapiens mRNA for protein-tyrosine-phosphatase (tissue type: testis)
AA630104	Lipase A, lysosomal acid, cholesterol esterase (Wolman disease)
AA454854	ALPHA-AMYLASE 2B PRECURSOR
W73406	DIHYDROPRYRIDINE-SENSITIVE L-TYPE, SKELETAL MUSCLE CALCIUM CHANNEL GAMMA SUBUNIT
R12802	Human cytochrome bc-1 complex core protein II mRNA, complete cds
AA465355	Homo sapiens mRNA for U3 snoRNP associated 55 kDa protein
AA829383	DUAL SPECIFICITY MITOGEN-ACTIVATED PROTEIN KINASE KINASE 3
AA629189	Keratin 4
AA430512	Homo sapiens cytoplasmic antiproteinase 3 (CAP3) mRNA, complete cds
AA456439	Human homozygous deletion target in pancreatic carcinoma (DPC4) mRNA, complete cds
H27864	SECRETOGRANIN II PRECURSOR
AA644657	MHC class I protein HLA-A (HLA-A28,-B40, -Cw3)
R40460	Homo sapiens phosphatidylinositol 4-kinase mRNA, complete cds
W96058	Human hnRNP H mRNA, complete cds
T72202	Human transcription factor IL-4 Stat mRNA, complete cds
AA598794	Connective tissue growth factor
AA599178	Ribosomal protein L27a
R88247	Adrenergic, beta, receptor kinase 1
T98612	Alpha-1 type 3 collagen
AA454856	Phospholipid hydroperoxide glutathione peroxidase
N67048	Type 3 iodothyronine deiodinase
AA778675	Homo sapiens mRNA for calmeglin, complete cds
H51117	Human calmodulin dependent phosphodiesterase PDE1B1 mRNA, complete cds
N36174	5-HYDROXYTRYPTAMINE 2B RECEPTOR
AA777187	Homo sapiens Cyr61 mRNA, complete cds
R09561	Decay accelerating factor for complement (CD55, Cromer blood group system)
R16849	Human HsPex13p mRNA, complete cds
AA884167	ANNEXIN XIII
AA136983	Cadherin 11 (OB-cadherin)
AA488622	Human signal transducing adaptor molecule STAM mRNA, complete cds
AA699427	Fructose-bisphosphatase 1
AA490459	Transcobalamin II
AA626787	Human ras-related C3 botulinum toxin substrate (rac) mRNA, complete cds
N62179	Human methylmalonate semialdehyde dehydrogenase gene, complete cds
N27190	UBIQUITIN CARBOXYL-TERMINAL HYDROLASE ISOZYME L3
AA441895	Human glutathione-S-transferase homolog mRNA, complete cds
AA463924	FACTOR VIII INTRON 22 PROTEIN
N78843	Homo sapiens cyclophilin-33A (CYP-33) mRNA, complete cds
AA629719	Cytochrome c oxidase VIIc subunit
AA464755	Ankyrin 1, erythrocytic
AA459351	H.sapiens sds22-like mRNA
AA488346	MYOSIN LIGHT CHAIN ALKALI, SMOOTH-MUSCLE ISOFORM
AA427899	Human mRNA fragment encoding beta-tubulin. (from clone D-beta-1)
AA453813	H.sapiens mRNA for Gal-beta(1-3/1-4)GlcNAc alpha-2.3-sialyltransferase
AA397824	Dopachrome tautomerase (dopachrome delta-isomerase, tyrosine-related protein 2)
AA633901	Transforming growth factor, beta-induced, 68kD
AA181334	Troponin I (skeletal fast)
AA292410	Clusterin (complement lysis inhibitor; testosterone-repressed prostate message 2; apolipoprotein J)
AA253434	HEAT SHOCK FACTOR PROTEIN 2
AA455056	H.sapiens mRNA for MAP kinase activated protein kinase

R55188	Human pre-T/NK cell associated protein (3B3) mRNA, 3' end
AA465723	Homo sapiens mRNA for protein phosphatase 2C gamma
N49856	SODIUM- AND CHLORIDE-DEPENDENT BETAIN TRANSPORTER
AA455272	H.sapiens mRNA for ITBA1 protein
AA459292	CDC28 protein kinase 1
AA878561	Ubiquitin A-52 residue ribosomal protein fusion product 1
AA772066	Human phosphatidylinositol (4,5)bisphosphate 5-phosphatase homolog mRNA, partial cds
N78621	H.sapiens mRNA for gamma-adaptin
AA291490	H.sapiens mRNA for processing a-glucosidase I
N46828	Homo sapiens mRNA for inositol 1,4,5-trisphosphate 3-kinase isoenzyme, partial cds
AA150487	Alkaline phosphatase, placental (Regan isozyme)
AA282537	MYOCYTE-SPECIFIC ENHANCER FACTOR 2
AA707922	Human mRNA for cone-specific cGMP phosphodiesterase gamma subunit, complete cds
AA443638	Homo sapiens breast cancer-specific protein 1 (BCSG1) mRNA, complete cds
W73892	Human putative tumor suppressor (LUCA15) mRNA, complete cds
N70734	Troponin T2 (cardiac)
H57136	Human phospholemman chloride channel mRNA, complete cds
AA709414	Nidogen (enactin)
W65461	Human protein tyrosine phosphatase mRNA, complete cds
AA436564	Human cellular proto-oncogene (c-met) mRNA, complete cds
AA029042	Human hSIAH2 mRNA, complete cds
AA427725	Homo sapiens carboxypeptidase Z precursor, mRNA, complete cds
N51280	ADP-ribosylation factor like 1
AA281347	H.sapiens mRNA for MHC class I promoter binding protein
AA402960	Human HLA class III region containing NOTCH4 gene, partial sequence, homeobox PBX2 (HPBX) gene, receptor for advanced glycosylation end products (RAGE) gene, complete cds, and 6 unidentified cds
N98485	Human forkhead protein FREAC-2 mRNA, partial cds
AA490209	H.sapiens mRNA for Sop2p-like protein
W61361	Homo sapiens cytoplasmic antiproteinase 2 (CAP2) mRNA, complete cds
N51018	Biglycan
AA455281	DEFENDER AGAINST CELL DEATH 1
W69471	V-ski avian sarcoma viral oncogene homolog
AA486321	Vimentin
AA458982	Solute carrier family 9 (sodium/hydrogen exchanger), isoform 1 (antiporter, Na <sup>+</sup> /H <sup>+</sup> , amiloride sensitive)
AA442095	NEDD-4 PROTEIN
N99003	Active BCR-related gene
AA609284	Homo sapiens mRNA for Eph-family protein, complete cds
AA195036	Human Ro/SSA ribonucleoprotein homolog (RoRet) mRNA, complete cds
AA478268	Human CtBP mRNA, complete cds
AA608583	Homo sapiens mRNA for OTK27, complete cds
AA486435	Homo sapiens mRNA for CDEP, complete cds
AA505045	Human L2-9 transcript of unrearranged immunoglobulin V(H)5 pseudogene
AA487893	TUMOR-ASSOCIATED ANTIGEN L6
AA292226	Homo sapiens creatine transporter mRNA, complete cds
H87106	Homo sapiens T245 protein (T245) mRNA, complete cds
W96450	Human putative tRNA synthetase-like protein mRNA, complete cds
N33331	Human peroxisome proliferator activated receptor mRNA, complete cds
AA405800	Dodecenoyl-Coenzyme A delta isomerase (3,2 trans-enoyl-Coenzyme A isomerase)
T51539	Macrophage stimulating 1 (hepatocyte growth factor-like)
N59764	Human guanosine 5'-monophosphate synthase mRNA, complete cds
AA521346	H.sapiens mRNA for Ndr protein kinase



AA428551	Homo sapiens SOX22 protein (SOX22) mRNA, complete cds
AA489383	Bone morphogenetic protein 2
AA490172	Collagen, type I, alpha-2
AA504477	Human cytoskeleton associated protein (CG22) mRNA, complete cds

## List of Table III related sequences:

Accession_	NAME	Gene
mrgd		
M98539	Human prostaglandin D2 synthase gene, exon 7	
AB004922	Homo sapiens gene for Smad 3, exon 1, partial sequence	
AB006000	Homo sapiens mRNA for chondromodulin-I precursor, complete cds	
AB017364	Homo sapiens mRNA for frizzled-2, complete cds	
AB020236	Homo sapiens gene for ribosomal protein L27A, complete cds	Ribosomal protein L27a
AB042820	Homo sapiens RPL6 gene for ribosomal protein L6, complete cds	Ribosomal protein L6
AB043547	Homo sapiens gene for SMAD4, partial cds	
AB080265	Homo sapiens CYP2J2 mRNA for cytochrome P450 2J2, complete cds	Cytochrome P450, subfamily IIJ (arachidonic acid epoxigenase) polypeptide 2
AF000979	Homo sapiens testis-specific Basic Protein Y 1 (BPY1) mRNA, complete cds	Homo sapiens testis-specific Basic Protein Y 1 (BPY1) mRNA, complete cds
AF001450	Homo sapiens core binding factor alpha1 subunit (CBFA1) gene, exon 7 and complete cds	
AF004231	Homo sapiens monocyte/macrophage Ig-related receptor MIR-10 (MIR cl-10) mRNA, complete cds	Homo sapiens monocyte/macrophage Ig-related receptor MIR-10 (MIR cl-10) mRNA, complete cds
AF009801	Homo sapiens homeodomain protein (BAPX1) mRNA, complete cds	
AF010126	Homo sapiens breast cancer-specific protein 1 (BCSG1) mRNA, complete cds	Homo sapiens breast cancer-specific protein 1 (BCSG1) mRNA, complete cds
AF010316	Homo sapiens Pig12 (PIG12) mRNA, complete cds	Homo sapiens Pig12 (PIG12) mRNA, complete cds
AF013591	Homo sapiens homolog of the Aspergillus nidulans sudD gene product mRNA, complete cds	Homo sapiens homolog of the Aspergillus nidulans sudD gene product mRNA, complete cds
AF037204	Homo sapiens RING zinc finger protein (RZF) mRNA, complete cds	
AF043339	Homo sapiens macrophage inflammatory protein 1 alpha (MIP1a) mRNA, partial cds	
AF049656	Homo sapiens inducible nitric oxide synthase (iNOS) mRNA, complete cds	
AF072872	Homo sapiens frizzled 1 mRNA, complete cds	
AF188285	Homo sapiens bone morphogenetic protein 9 (BMP9) mRNA, complete cds	
AF189279	Homo sapiens group IIE secretory phospholipase A2 mRNA, complete cds	
AF248634	Homo sapiens syndecan 3 (SDC3) mRNA, complete cds	
AF304431	Homo sapiens hypoxia-inducible factor 1 alpha subunit (HIF1A) mRNA, complete cds	

AF339054	Homo sapiens BCL2-associated X protein (BAX) gene, exons 1, 2 and partial cds	
AF348700	Homo sapiens ubiquitin A-52 residue ribosomal protein fusion product 1 (UBA52), mRNA, complete cds	Ubiquitin A-52 residue ribosomal protein fusion product 1
AF395008	Homo sapiens Interleukin 4 (IL4) gene, complete cds	
AF405705	Homo sapiens matrix metalloproteinase 3 (stromelysin 1, progelatinase) (MMP3) gene, complete cds	
AF411526	Homo sapiens nerve growth factor beta (NGFB) mRNA, complete cds	Nerve growth factor beta
AF469046	Homo sapiens macrophage migration inhibitory factor (MIF) mRNA, complete cds	
AF477981	Homo sapiens osterix mRNA, complete cds	
AJ279016	Homo sapiens mRNA for chondrocyte expressed protein 68 kDa (CEP-68 gene)	
AY043326	Homo sapiens keratin 4 (KRT4) gene, complete cds	Keratin 4
AY044847	Homo sapiens aggrecanase 1 (ADAMTS4) gene, complete cds	
D13748	Human mRNA for eukaryotic initiation factor 4A1	Human mRNA for eukaryotic initiation factor 4A1
D38255	Homo sapiens mRNA for CAB1, complete cds	Homo sapiens mRNA for CAB1, complete cds
D45399	Human mRNA for cone-specific cGMP phosphodiesterase gamma subunit, complete cds	Human mRNA for cone-specific cGMP phosphodiesterase gamma subunit, complete cds
D49738	Human cytoskeleton associated protein (CG22) mRNA, complete cds	Human cytoskeleton associated protein (CG22) mRNA, complete cds
D49835	Homo sapiens mRNA for DNA-binding protein, complete cds	Homo sapiens mRNA for DNA-binding protein, complete cds
D90040	Human mRNA for arylamine N-acetyltransferase (EC 2.3.1.5)	ARYLAMINE N-ACETYLTRANSFERASE, MONOMORPHIC
J00306	Human somatostatin I gene and flanks	Human somatostatin I gene and flanks
J03191	Human profilin mRNA, complete cds	Human profilin mRNA, complete cds
J03592	Human ADP/ATP translocase mRNA, 3' end, clone pHAT8	Human ADP/ATP translocase mRNA, 3' end, clone pHAT8
J04111	Human c-jun proto oncogene (JUN), complete cds, clone hCJ-1	
J04177	Human alpha-1 type XI collagen (COL11A1) mRNA, complete cds	
J04973	Human cytochrome bc-1 complex core protein II mRNA, complete cds	Human cytochrome bc-1 complex core protein II mRNA, complete cds
J05036	Human cathepsin E mRNA, complete cds	Cathepsin E
K00065	Human superoxide dismutase (SOD-1) mRNA, complete cds	Human superoxide dismutase (SOD-1) mRNA, complete cds
K00650	Human fos proto-oncogene (c-fos), complete cds	
L05095	Homo sapiens ribosomal protein L30 mRNA, complete cds	60S RIBOSOMAL PROTEIN L30
L08895	Homo sapiens MADS/MEF2-family transcription factor (MEF2C) mRNA, complete cds	
L10347	Human pro-alpha1 type II collagen (COL2A1) gene exons 1-54, complete cds	
L11566	Homo sapiens ribosomal protein L18 (RPL18) mRNA, complete cds	60S RIBOSOMAL PROTEIN L18

L13286	Human mitochondrial 1,25-dihydroxyvitamin D3 24-hydroxylase mRNA, complete cds	Human mitochondrial 1,25-dihydroxyvitamin D3 24-hydroxylase mRNA, complete cds
L13463	Human helix-loop-helix basic phosphoprotein (G0S8) mRNA, complete cds	
L13616	Human focal adhesion kinase (FAK) mRNA, complete cds	
L13720	Homo sapiens growth-arrest-specific protein (gas) mRNA, complete cds	Homo sapiens growth-arrest-specific protein (gas) mRNA, complete cds
L22009	Human hnRNP H mRNA, complete cds	Human hnRNP H mRNA, complete cds
L28997	Homo sapiens ARL1 mRNA, complete cds	ADP-ribosylation factor like 1
L31409	Homo sapiens creatine transporter mRNA, complete cds	Homo sapiens creatine transporter mRNA, complete cds
L33930	Homo sapiens CD24 signal transducer mRNA, complete cds and 3' region	
L34059	Homo sapiens cadherin-4 mRNA, complete cds	
L41162	Homo sapiens collagen alpha 3 type IX (COL9A3) mRNA, complete cds	
L47647	Homo sapiens creatine kinase B mRNA, complete cds	Creatine kinase B
M13994	Human B-cell leukemia/lymphoma 2 (bcl-2) proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds	bcl-2-alpha protein, complete cds
M14144	Human vimentin gene, complete cds	Vimentin
M14631	Human guanine nucleotide-binding protein G-s, alpha subunit mRNA, partial cds	Human guanine nucleotide-binding protein G-s, alpha subunit mRNA, partial cds
M16652	Human pancreatic elastase IIA mRNA, complete cds	Elastase 1, pancreatic (elastase IIA)
M20137	Human interleukin 3 (IL-3) mRNA, complete cds, clone pcD-SR-alpha	
M22636	Human U1 small nuclear ribonucleoprotein 70 kd protein mRNA, complete cds	U1 snRNP 70K protein
M37825	Human fibroblast growth factor-5 (FGF-5) mRNA, complete cds	
M57293	Human parathyroid hormone-related peptide (PTHrP) gene, exons 1A, 1B, 1C, and 2	Ribosomal protein S4, X-linked
M58458	Human ribosomal protein S4 (RPS4X) isoform mRNA, complete cds	Homo sapiens catechol-O-methyltransferase (COMT) mRNA, complete cds
M58525	Homo sapiens catechol-O-methyltransferase (COMT) mRNA, complete cds	
M58549	Human matrix Gla protein (MGP) mRNA, complete cds	
M61877	Human erythroid alpha-spectrin (SPTA1) mRNA, complete cds	Erythroid alpha-spectrin
M62402	Human insulin-like growth factor binding protein 6 (IGFBP6) mRNA, complete cds	Insulin-like growth factor binding protein 6
M65062	Human insulin-like growth factor binding protein 5 (IGFBP-5) mRNA, complete cds	
M65217	Human heat shock factor 2 (HSF2) mRNA, complete cds	HEAT SHOCK FACTOR PROTEIN 2
M76701	Homo sapiens zinc finger protein 35 (ZNF35) gene, exon 1	
M77016	Human tropomodulin mRNA, complete cds	Tropomodulin

M81768	Human Na/H antiporter (APNH1) mRNA, complete cds	Human Na/H antiporter (APNH1) mRNA, complete cds
M84489	Human extracellular signal-regulated kinase 2 mRNA, complete cds	
M84721	Human AMP deaminase (AMPD3) mRNA, complete cds	Adenosine monophosphate deaminase (isoform E)
M87842	Human S-lac lectin L-14-II (LGALS2) mRNA, complete cds	GALECTIN-2
M92934	Human connective tissue growth factor, complete cds	Connective tissue growth factor
M95610	Human alpha 2 type IX collagen (COL9A2) mRNA, partial cds	
M96684	H.sapiens Pur (pur-alpha) mRNA, complete cds	H.sapiens Pur (pur-alpha) mRNA, complete cds
M97676	Homo sapiens (region 7) homeobox protein (HOX7) mRNA, complete cds	
NM_000194	Homo sapiens hypoxanthine phosphoribosyltransferase 1 (Lesch-Nyhan syndrome) (HPR1), mRNA	
NM_000213	Homo sapiens integrin, beta 4 (ITGB4), mRNA	
NM_000221	Homo sapiens ketohexokinase (fructokinase) (KHK), transcript variant a, mRNA	H.sapiens KHK mRNA for ketohexokinase, clone pHKHK3a
NM_000235	Homo sapiens lipase A, lysosomal acid, cholesterol esterase (Wolman disease) (LIPA), mRNA	Lipase A, lysosomal acid, cholesterol esterase (Wolman disease)
NM_000358	Homo sapiens transforming growth factor, beta-induced, 68kD (TGFB1), mRNA	Transforming growth factor, beta-induced, 68kD
NM_000364	Homo sapiens troponin T2, cardiac (TNNT2), mRNA	Troponin T2 (cardiac)
NM_000537	Homo sapiens renin (REN), mRNA	RENIN PRECURSOR, RENAL
NM_000574	Homo sapiens decay accelerating factor for complement (CD55, Cromer blood group system) (DAF), mRNA	Decay accelerating factor for complement (CD55, Cromer blood group system)
NM_000600	Homo sapiens Interleukin 6 (Interferon, beta 2) (IL6), mRNA	
NM_000618	Homo sapiens insulin-like growth factor 1 (somatomedin C) (IGF1), mRNA	
NM_000632	Homo sapiens Integrin, alpha M (complement component receptor 3, alpha; also known as CD11b (p170), macrophage antigen alpha polypeptide) (ITGAM), mRNA	Integrin, alpha M (complement component receptor 3, alpha; also known as CD11b (p170), macrophage antigen alpha polypeptide)
NM_000711	Homo sapiens bone gamma-carboxyglutamate (gla) protein (osteocalcin) (BGLAP), mRNA	
NM_000962	Homo sapiens prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase) (PTGS1), transcript variant 1, mRNA	Prostaglandin-endoperoxide synthase 1 (prostaglandin G/H synthase and cyclooxygenase)
NM_000977	Homo sapiens ribosomal protein L13 (RPL13), transcript variant 1, mRNA	60S RIBOSOMAL PROTEIN L13
NM_000996	Homo sapiens ribosomal protein L35a (RPL35A), mRNA	Ribosomal protein L35a
NM_001012	Homo sapiens ribosomal protein S8 (RPS8), mRNA	40S RIBOSOMAL PROTEIN S8
NM_001025	Homo sapiens ribosomal protein S23 (RPS23), mRNA	40S RIBOSOMAL PROTEIN S23
NM_001064	Homo sapiens transketolase (Wernicke-Korsakoff syndrome) (TKT), mRNA	Transketolase (Wernicke-Korsakoff syndrome)
NM_001127	Homo sapiens adaptor-related protein complex 1, beta 1 subunit	Adaptin, beta 1 (beta prime)

NM_001200	Homo sapiens bone morphogenetic protein 2 (BMP2), mRNA	AP1B1), mRNA
NM_001229	Homo sapiens caspase 9, apoptosis-related cysteine protease (CASP9), transcript variant alpha, mRNA	Bone morphogenetic protein 2
NM_001511	Homo sapiens GRO1 oncogene (melanoma growth stimulating activity, alpha) (GRO1), mRNA	transcript variant alpha, mRNA
NM_001565	Homo sapiens small inducible cytokine subfamily B (Cys-X-Cys), member 10 (SCYB10), mRNA	Interferon (gamma)-induced cell line; protein 10 from
NM_001632	Homo sapiens alkaline phosphatase, placental (Regan isozyme) (ALPP), mRNA	Alkaline phosphatase, placental (Regan isozyme)
NM_001687	Homo sapiens ATP synthase, H+ transporting, mitochondrial F1 complex, delta subunit (ATP5D), mRNA	ATP synthase, H+ transporting, mitochondrial F1 complex, delta subunit
NM_001718	Homo sapiens bone morphogenetic protein 6 (BMP6), mRNA	Calcium modulating ligand
NM_001745	Homo sapiens calcium modulating ligand (CAMLG), mRNA	transcript variant 1, mRNA
NM_001797	Homo sapiens cadherin 11, type 2, OB-cadherin (osteoblast) (CDH11), mRNA	transcript variant 1, mRNA
NM_001844	Homo sapiens collagen, type II, alpha 1 (primary osteoarthritis, spondyloepiphyseal dysplasia, congenital) (COL2A1), mRNA	transcript variant 1, mRNA
NM_001912	Homo sapiens cathepsin L (CTSL), mRNA	
NM_001969	Homo sapiens eukaryotic translation initiation factor 5 (EIF5), mRNA	Eukaryotic translation initiation factor 5 (eIF5)
NM_002073	Homo sapiens guanine nucleotide binding protein (G protein), alpha z polypeptide (GNAZ), mRNA	Guanine nucleotide binding protein (G protein), alpha z polypeptide
NM_002094	Homo sapiens G1 to S phase transition 1 (GSPT1), mRNA	G1 to S phase transition 1
NM_002160	Homo sapiens hexabrachion (tenascin C, cytactin) (HXB), mRNA	
NM_002211	Homo sapiens integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12) (ITGB1), mRNA	
NM_002379	Homo sapiens matrilin 1, cartilage matrix protein (MATN1), mRNA	
NM_002381	Homo sapiens matrilin 3 (MATN3) precursor, mRNA	
NM_002421	Homo sapiens matrix metalloproteinase 1 (interstitial collagenase) (MMP1), mRNA	
NM_002424	Homo sapiens matrix metalloproteinase 8 (neutrophil collagenase) (MMP8), mRNA	
NM_002427	Homo sapiens matrix metalloproteinase 13 (collagenase 3) (MMP13), mRNA	
NM_002591	Homo sapiens phosphoenolpyruvate carboxykinase 1 (soluble) (PCK1), mRNA	Phosphoenolpyruvate carboxykinase 1 (soluble) mRNA
NM_002619	Homo sapiens platelet factor 4 (PF4), mRNA	Platelet factor 4
NM_002722	Homo sapiens pancreatic polypeptide (PPY), mRNA	
NM_002738	Homo sapiens protein kinase C, beta 1 (PRKCB1), mRNA	Protein kinase C, beta 1
NM_002903	Homo sapiens recoverin (RCV1), mRNA	Recoverin

NM_003036	Homo sapiens v-ski sarcoma viral oncogene homolog (avian) (SKI), mRNA	V-ski avian sarcoma viral oncogene homolog
NM_003282	Homo sapiens troponin I, skeletal, fast (TNNT2), mRNA	Troponin I (skeletal fast)
NM_003385	Homo sapiens visinin-like 1 (VSNL1),	Visinin-like 1
NM_003395	Homo sapiens wingless-type MMTV integration site family, member 14 (WNT14), mRNA	mRNA
NM_004613	Homo sapiens transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase) (TGM2), mRNA	mRNA
NM_004832	Homo sapiens glutathione-S-transferase like; glutathione transferase omega (GSTT1p28), mRNA	Human glutathione-S-transferase homolog mRNA, complete cds
NM_004994	Homo sapiens matrix metalloproteinase 9 (gelatinase B, 92kD gelatinase, 92kD type IV collagenase) (MMP9), mRNA	mRNA
NM_004995	Homo sapiens matrix metalloproteinase 14 (membrane-inserted) (MMP14), mRNA	mRNA
NM_005038	Homo sapiens peptidylprolyl isomerase D (cyclophilin D) (PPID), mRNA	40 KD PEPTIDYL-PROLYL CIS-TRANS ISOMERASE
NM_005186	Homo sapiens calpain 1, (mu/l) large subunit (CAPN1), mRNA	CALPAIN 1, LARGE
NM_005346	Homo sapiens heat shock 70kD protein 1B (HSPA1B), mRNA	HEAT SHOCK 70 KD PROTEIN 1
NM_005438	Homo sapiens FOS-like antigen 1 (FOSL1), mRNA	
NM_005506	Homo sapiens CD36 antigen (collagen type I receptor, thrombospondin receptor)-like 2 (lysosomal integral membrane protein II) (CD36L2), mRNA	
NM_006289	Homo sapiens talin 1 (TLN1), mRNA	
NM_006988	Homo sapiens a disintegrin-like and metalloprotease (repolydin type) with thrombospondin type 1 motif, 1 (ADAMTS1), mRNA	
NM_007306	Homo sapiens breast cancer 1, early onset (BRCA1), transcript variant BRCA1-exon4, mRNA	Breast cancer 1, early onset
NM_007352	Homo sapiens elastase 3B, pancreatic (ELA3B), Mrna	ELASTASE IIIB PRECURSOR
NM_014000	Homo sapiens vinculin (VCL), transcript variant meta-VCL, mRNA	
NM_014470	Homo sapiens GTP-binding protein (RHO6), mRNA	
NM_018952	Homo sapiens homeo box B6 (HOXB6), mRNA	
NM_021019	Homo sapiens myosin, light polypeptide 6, alkali, smooth muscle and non-muscle (MYL6), transcript variant 1, mRNA	MYOSIN LIGHT CHAIN ALKALI, SMOOTH-MUSCLE ISOFORM
NM_033150	Homo sapiens collagen, type II, alpha 1 (primary osteoarthritis, spondyloepiphyseal dysplasia, congenital) (COL2A1), transcript variant 2, mRNA	
NM_053056	Homo sapiens cyclin D1 (PRAD1; parathyroid adenomatosis 1) (CCND1), mRNA	Cyclin D1 (PRAD1; parathyroid adenomatosis 1)
NM_080682	Homo sapiens vascular cell adhesion molecule 1 (VCAM1), transcript variant 2, mRNA	
S79854	Homo sapiens type 3 iodothyronine deiodinase mRNA, complete cds	Type 3 iodothyronine deiodinase
S83308	SOX5=Sry-related HMG box gene (alternatively spliced) [human, testis, mRNA, 1473 nt]	
U07424	Human putative tRNA synthetase-like protein mRNA, complete cds	Human putative tRNA synthetase-like protein mRNA, complete cds

U07620	Human MAP kinase mRNA, complete cds	Human MAP kinase mRNA, complete cds
U08023	Human cellular proto-oncogene (c-met) mRNA, complete cds	Human cellular proto-oncogene (c-met) mRNA, complete cds
U09303	Human T cell leukemia LERK-2 (EPLG2) mRNA, complete cds	
U09577	Homo sapiens lysosomal hyaluronidase (LUCA2/HYAL2) mRNA, complete cds	Human PH-20 homolog (LUCA2) mRNA, partial cds
U09825	Human acid finger protein mRNA, complete cds	Acid finger protein ZNF173
U13261	Homo sapiens eIF-2-associated p67 homolog mRNA, complete cds	Human eIF-2-associated p67 homolog mRNA, complete cds
U13660	Human cartilage-derived morphogenetic protein 1 (CDMP-1) mRNA, complete cds	
U13991	Human TATA-binding protein associated factor 30 kDa subunit (tafl130) mRNA, complete cds	Human TATA-binding protein associated factor 30 kDa subunit (tafl130) mRNA, complete cds
U14966	Human ribosomal protein L5 mRNA, complete cds	Ribosomal protein L5
U14971	Human ribosomal protein S9 mRNA, complete cds	
U15085	Human HLA-DMB mRNA, complete cds	Major histocompatibility complex, class II, DM beta
U16031	Human transcription factor IL-4 Stat mRNA, complete cds	Human transcription factor IL-4 Stat mRNA, complete cds
U16261	Human MDA-7 (mda-7) mRNA, complete cds	
U18299	Human damage-specific DNA binding protein DDBa p127 subunit (DDB1) mRNA, complete cds	Damage-specific DNA binding protein 1 (127 kD)
U20980	Human chromatin assembly factor-I p60 subunit mRNA, complete cds	Human chromatin assembly factor-I p60 subunit mRNA, complete cds
U22409	Human parathyroid hormone/PTH-related peptide receptor (PTH/PTHrP) gene, exon 14 and complete cds	
U23028	Human eukaryotic initiation factor 2B-epsilon mRNA, partial cds	Human eukaryotic initiation factor 2B-epsilon mRNA, partial cds
U23946	Human putative tumor suppressor (LUCA15) mRNA, complete cds	Human putative tumor suppressor (LUCA15) mRNA, complete cds
U24152	Human p21-activated protein kinase (Pak1) gene, complete cds	Human protein kinase PAK1 mRNA, complete cds
U25789	Human ribosomal protein L21 mRNA, complete cds	Ribosomal protein L21
U27699	Human pephBGT-1 betaine-GABA transporter mRNA, complete cds	SODIUM- AND CHLORIDE-DEPENDENT BETAIN TRANSPORTER
U31202	Human noggin (NOGGIN) gene, complete cds, (NOG)	
U32169	Human pro-a2 chain of collagen type XI (COL11A2) gene, complete cds	
U32907	Human p37NB mRNA, complete cds	Human p37NB mRNA, complete cds
U33822	Human tax1-binding protein TXBP181 mRNA, complete cds	Human tax1-binding protein TXBP181 mRNA, complete cds
U37012	Human cleavage and polyadenylation specificity factor mRNA, complete cds	Human cleavage and polyadenylation specificity factor mRNA, complete cds
U38864	Human zinc-finger protein C2H2-150 mRNA, complete cds	Human zinc-finger protein C2H2-150 mRNA, complete cds



U40373	Human cell surface glycoprotein CD44 mRNA, complete cds	AQUAPORIN-CHIP
U41517	Human channel-like integral membrane protein (AQP-1) mRNA, clone AQP-1-1656, complete cds	
U43148	Human patched homolog (PTC) mRNA, complete cds	Friedreich ataxia
U43747	Human frataxin (FRDA) mRNA, complete cds	Bone morphogenetic protein 4
U43842	Homo sapiens bone morphogenetic protein-4 (hBMP-4) gene, complete cds	
U45975	Human phosphatidylinositol (4,5)bisphosphate 5-phosphatase homolog mRNA, partial cds	Human phosphatidylinositol (4,5)bisphosphate 5-phosphatase homolog mRNA, partial cds
U53204	Human plectin (PLEC1) mRNA, complete cds	Human plectin (PLEC1) mRNA, complete cds
U53347	Human neutral amino acid transporter B mRNA, complete cds	Human neutral amino acid transporter B mRNA, complete cds
U59289	Human H-cadherin mRNA, complete cds	
U59423	Human Smad1 mRNA, complete cds	
U63717	Homo sapiens osteoclast stimulating factor mRNA, complete cds	Human osteoclast stimulating factor mRNA, complete cds
U68723	Human checkpoint suppressor 1 mRNA, complete cds	
U70312	Homo sapiens integrin binding protein Del-1 (Delt) mRNA, complete cds	
U72245	Human phospholemman chloride channel mRNA, complete cds	Human phospholemman chloride channel mRNA, complete cds
U75283	Human sigma receptor mRNA, complete cds	Human sigma receptor mRNA, complete cds
U76992	Human Tat-SF1 mRNA, complete cds	Human Tat-SF1 mRNA, complete cds
U80998	Human basic helix-loop-helix DNA binding protein (TWIST) gene, complete cds	
U83460	Human high-affinity copper uptake protein (hCTR1) mRNA, complete cds	Human high-affinity copper uptake protein (hCTR1) mRNA, complete cds
U90547	Human Ro/SSA ribonucleoprotein homolog (RoRet) mRNA, complete cds	Human Ro/SSA ribonucleoprotein homolog (RoRet) mRNA, complete cds
U92268	Homo sapiens mitogen activated protein kinase p38-2 mRNA, complete cds	
U93181	Homo sapiens nuclear dual-specificity phosphatase (SBF1) mRNA, partial cds	Homo sapiens nuclear dual-specificity phosphatase (SBF1) mRNA, partial cds
X00129	Human mRNA for retinol binding protein (RBP)	
X00588	Human mRNA for precursor of epidermal growth factor receptor	
X02910	Human gene for tumor necrosis factor (TNF-alpha)	
X03742	Human gene for L apoferritin exons 1 and 2	
X04412	Human mRNA for plasma gelsolin	GELSOLIN PRECURSOR, PLASMA
X06614	Human mRNA for receptor of retinoic acid	Human mRNA for receptor of retinoic acid

X12794	Human v-erbA related ear-2 gene	Human v-erbA related ear-2 gene
X14420	Human mRNA for pro-alpha-1 type 3 collagen	
X51801	Human OP-1 mRNA for osteogenic protein	
X54412	Human mRNA for alpha1(IX) collagen (long form)	
X55654	Homo sapiens mitochondrial coxII mRNA for cytochrome C oxidase II subunit	
X55764	Human mRNA for cytochrome P-450 (11 Beta)	Cytochrome P450 11 beta
X58399	Human L2-9 transcript of unrearranged immunoglobulin V(H)5 pseudogene	Human L2-9 transcript of unrearranged immunoglobulin V(H)5 pseudogene
X58957	H.sapiens alk mRNA for agammaglobulinaemia tyrosine kinase	Agammaglobulinaemia protein-tyrosine kinase alk
X60188	Human ERK1 mRNA for protein serine/threonine kinase	
X60382	H.sapiens COL10A1 gene for collagen (alpha-1 type X)	
X67337	H.sapiens HPBR11-4 mRNA	H.sapiens HPBR11-4 mRNA
X70683	H.sapiens mRNA for SOX-4 protein	
X71661	H.sapiens ERGIC-53 mRNA	ERGIC-53 PROTEIN PRECURSOR
X74795	H.sapiens P1-Cdc46 mRNA	CDC46 HOMOLOG
X76770	H.sapiens PAP mRNA	H.sapiens PAP mRNA
X78712	H.sapiens mRNA for glycerol kinase testis specific 2	Glycerol kinase 2 (testis specific)
X87237	H.sapiens mRNA for processing a-glucosidase I	H.sapiens mRNA for processing a-glucosidase I
X87342	H.sapiens mRNA for human giant larvae homolog	H.sapiens mRNA for human giant larvae homolog
X92475	H.sapiens mRNA for ITBA1 protein	H.sapiens mRNA for ITBA1 protein
X94216	H.sapiens mRNA for VEGF-C protein	
XM_001306	Homo sapiens solute carrier family 16 (monocarboxylic acid transporters), member 1 (SLC16A1), mRNA	Solute carrier family 16 (monocarboxylic acid transporters), member 1
XM_001316	Homo sapiens adenosine monophosphate deaminase 1 (isoform M) (AMPD1), mRNA	Adenosine monophosphate deaminase 1 (isoform M)
XM_001324	Homo sapiens calponin 3, acidic (CNN3), mRNA	Calponin 3, acidic
XM_001782	Homo sapiens fibromodulin (FMOD), mRNA	
XM_001826	Homo sapiens alkaline phosphatase, liver/bone/kidney (ALPL), mRNA	Alkaline phosphatase, liver/bone/kidney
XM_002321	Homo sapiens glypican 1 (GPC1), mRNA	Glypican 1
XM_003059	Homo sapiens peroxisome proliferative activated receptor, gamma (PPARG), mRNA	
XM_003222	Homo sapiens catenin (cadherin-associated protein), beta 1 (88kD) (CTNNB1), mRNA	
XM_003730	Homo sapiens cytochrome c oxidase subunit VIc (COX7C), mRNA	Cytochrome c oxidase VIc subunit
XM_003752	Homo sapiens interleukin 3 (colony-stimulating factor, multiple) (IL3), mRNA	

XM_003913	Homo sapiens integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor) (ITGA2), mRNA	
XM_004063	Homo sapiens early growth response 1 (EGR1), mRNA	
XM_006121	Homo sapiens cathepsin D (lysosomal aspartyl protease) (CTSD), mRNA	
XM_009336	Homo sapiens cartilage oligomeric matrix protein (pseudoachondroplasia, epiphyseal dysplasia 1, multiple) (COMP), mRNA	
XM_009915	Homo sapiens leukemia inhibitory factor (cholinergic differentiation factor) (LIF), mRNA	
XM_010702	Homo sapiens cathepsin K (pseudosyndostosis) (CTSK), mRNA	
XM_012503	Homo sapiens matrix metalloproteinase 2 (gelatinase A, 72kD gelatinase, 72kD type IV collagenase) (MMP2), mRNA	
XM_012651	Homo sapiens collagen, type I, alpha 1 (COL1A1), mRNA	
XM_015434	Homo sapiens chitinase 3-like 1 (cartilage glycoprotein-39) (CHI3L1), mRNA	
XM_016181	Homo sapiens wingless-type MMTV integration site family, member 5A (WNT5A), mRNA	
XM_017096	Homo sapiens active BCR-related gene (ABR), mRNA	
XM_017384	Homo sapiens matrix metalloproteinase 7 (matrilysin, uterine) (MMP7), mRNA	Matrix metalloproteinase 7 (matrilysin, uterine)
XM_017591	Homo sapiens annexin A6 (ANXA6), mRNA	Annexin VI (p88)
XM_028204	Homo sapiens nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 (p105) (NFKB1), mRNA	
XM_028642	Homo sapiens integrin, alpha 5 (fibronectin receptor, alpha polypeptide) (ITGA5), mRNA	
XM_029245	Homo sapiens collagen, type I, alpha 2 (COL1A2), mRNA	Collagen, type I, alpha-2
XM_029796	Homo sapiens frizzled-related protein (FRZB), mRNA	
XM_031221	Homo sapiens interleukin 1, alpha (IL1A), mRNA	
XM_031288	Homo sapiens aggrecan 1 (chondroitin sulfate proteoglycan 1, large aggregating proteoglycan, antigen identified by monoclonal antibody A0122) (AGC1), mRNA	
XM_031289	Homo sapiens interleukin 8 (IL8), mRNA	
XM_032902	Homo sapiens integrin, alpha 1 (ITGA1), mRNA	
XM_033470	Homo sapiens defender against cell death 1 (DAD1), mRNA	DEFENDER AGAINST CELL DEATH 1
XM_033657	Homo sapiens heparan sulfate proteoglycan 2 (perlecan) (HSPG2), mRNA	
XM_033878	Homo sapiens tissue inhibitor of metalloproteinase 1 (erythroid potentiating activity, collagenase inhibitor) (TIMP1), mRNA	
XM_034023	Homo sapiens tissue inhibitor of metalloproteinase 1 (erythroid potentiating activity, collagenase inhibitor) (TIMP1), mRNA	Human RGP4 mRNA, complete cds
XM_034556	Homo sapiens regulator of G-protein signalling 4 (RGS4), mRNA	
XM_034845	Homo sapiens chloride channel 7 (CLCN7), mRNA	
	Homo sapiens phosphatase and tensin homolog (mutated in multiple advanced cancers 1) (PTEN), mRNA	Phosphatase and tensin homolog (mutated in multiple advanced cancers 1)
XM_034890	Homo sapiens fibrillin 1 (Marfan syndrome) (FBN1), mRNA	
XM_035662	Homo sapiens cathepsin B (CTSB), mRNA	
XM_035842	Homo sapiens small inducible cytokine A5 (RANTES) (SCYA5), mRNA	Small inducible cytokine A5 (RANTES)
XM_036107	Homo sapiens integrin, beta 2 (antigen CD18 (p95), lymphocyte function-associated antigen 1; macrophage antigen 1 (mac-1) beta subunit)	

	(ITGB2), mRNA	
XM_036175	Homo sapiens collagen, type XVIII, alpha 1 (COL18A1), mRNA	Collagen, type XVIII, alpha 1
XM_037087	Homo sapiens ATP binding protein associated with cell differentiation (APACD), mRNA	Homo sapiens mRNA for ATP binding protein, complete cds
XM_037646	Homo sapiens msh homeo box homolog 2 (Drosophila) (MSX2), mRNA	
XM_037965	Homo sapiens chondroadherin (CHAD), mRNA	
XM_038584	Homo sapiens tissue inhibitor of metalloproteinase 3 (Sorsby fundus dystrophy, pseudoinflammatory) (TIMP3), mRNA	
XM_039094	Homo sapiens SRY (sex determining region Y)-box 9 (campomelic dysplasia, autosomal sex-reversal) (SOX9), mRNA	
XM_040037	Homo sapiens adrenergic, beta, receptor kinase 1 (ADRBK1), mRNA	Adrenergic, beta, receptor kinase 1
XM_040385	Homo sapiens S-adenosylmethionine decarboxylase 1 (AMD1), mRNA	S-adenosylmethionine decarboxylase 1
XM_042153	Homo sapiens biglycan (BGN), mRNA	Biglycan
XM_042664	Homo sapiens nuclear autoantigenic sperm protein (histone-binding) (NASP), mRNA	Nuclear autoantigenic sperm protein (histone-binding)
XM_044120	Homo sapiens fibroblast growth factor receptor 3 (achondroplasia, thanatophoric dwarfism) (FGFR3), mRNA	
XM_045089	Homo sapiens ATPase, Cu++ transporting, beta polypeptide (Wilson disease) (ATP7B), mRNA	ATPase, Cu++ transporting, beta polypeptide (Wilson disease)
XM_045802	Homo sapiens paxillin (PXN), Mima	
XM_045890	Homo sapiens ADP-ribosylation factor 4-like (ARF4L), mRNA	ADP-ribosylation factor 4-like
XM_045925	Homo sapiens decorin (DCN), mRNA	Decorin
XM_045926	Homo sapiens lumican (LUM), mRNA	
XM_046035	Homo sapiens integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide) (ITGAL), mRNA	Integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)
XM_046758	Homo sapiens tensin (TNS), mRNA	
XM_046765	Homo sapiens thymidylate synthetase (TYMS), mRNA	Thymidylate synthase
XM_047231	Homo sapiens fibulin 1 (FBLN1), mRNA	
XM_047719	Homo sapiens transcription factor 7 (T-cell specific, HMG-box) (TCF7), mRNA	Transcription factor 7 (T-cell specific)
XM_047802	Homo sapiens a disintegrin-like and metalloprotease (repolydin type) with thrombospondin type 1 motif, 5 (aggrecaanse-2) (ADAMTS5), mRNA	
XM_048167	Homo sapiens troponin T1, skeletal, slow (TNNT1), mRNA	Troponin T1, skeletal, slow
XM_048201	Homo sapiens metallothionein 1L (MT1L), mRNA	Metallothionein 1L
XM_049177	Homo sapiens vascular endothelial growth factor B (VEGFB), mRNA	
XM_049518	Homo sapiens intercellular adhesion molecule 1 (CD54), human rhinovirus receptor (ICAM1), mRNA	Intercellular adhesion molecule 1 (CD54), human rhinovirus receptor

XM_049534	Homo sapiens amylase, alpha 2A; pancreatic (AMY2A), mRNA	Amylase, alpha 2A; pancreatic
XM_049690	Homo sapiens coatomer protein complex, subunit alpha (COPA), mRNA	Human coatomer protein (HEPCOP) mRNA, complete cds
XM_049864	Homo sapiens colony stimulating factor 3 (granulocyte) (CSF3), mRNA	
XM_049937	Homo sapiens insulin-like growth factor binding protein 4 (IGFBP4), mRNA	
XM_050846	Homo sapiens Indian hedgehog homolog (Drosophila) (IHH), mRNA	
XM_053809	Homo sapiens similar to chondroitin sulfate proteoglycan 2 (versican) (H. sapiens) (LOC153633), mRNA	
XM_054566	Homo sapiens collagen, type VI, alpha 1 (COL6A1), mRNA	
XM_054686	Homo sapiens caspase 3, apoptosis-related cysteine protease (CASP3), mRNA	
XM_055254	Homo sapiens fibronectin 1 (FN1), mRNA	
XM_058069	Homo sapiens matrix metalloproteinase 12 (macrophage elastase) (MMP12), mRNA	
XM_084239	Homo sapiens retinoic acid receptor responder (tazarotene induced) 2 Human tazarotene-induced gene 2 (TIG2) mRNA, complete cds	
XM_084263	(RARRES2), Mrna	
XM_084263	Homo sapiens cytochrome c oxidase subunit VIc (COX6C), mRNA	Human mRNA for cytochrome c oxidase subunit VIc
XM_084285	Homo sapiens integral membrane protein 2A (ITM2A), mRNA	
XM_085705	Homo sapiens tissue inhibitor of metalloproteinase 2 (TIMP2), mRNA	
XM_086368	Homo sapiens MUF1 protein (MUF1), mRNA	H.sapiens mRNA for MUF1 protein
XM_096277	Homo sapiens collagen, type V, alpha 1 (COL5A1), mRNA	
Y00985	Human mRNA for manganese-containing superoxide dismutase	
Y07566	H.sapiens mRNA for RIT protein	H.sapiens mRNA for RIT protein
Y07570	H.sapiens mRNA for PHAP12b protein	H.sapiens mRNA for PHAP12b protein
Y08999	H.sapiens mRNA for Sop2p-like protein	H.sapiens mRNA for Sop2p-like protein
Y12692	Homo sapiens mRNA for WNT11 gene	
Y13936	Homo sapiens mRNA for protein phosphatase 2C gamma	Homo sapiens mRNA for protein phosphatase 2C gamma
Y15227	Homo sapiens mRNA for leukemia associated gene 1	Homo sapiens mRNA for leukemia associated gene 1
Z22865	H.sapiens dermatopontin mRNA, complete CDS	
Z50781	H.sapiens mRNA for leucine zipper protein	
Z50853	H.sapiens mRNA for CLPP	H.sapiens mRNA for CLPP

The current invention also encompasses the process of down compression of previously determined 467 genes to a lower number that is still able to characterize the desired number of different cellular status. At present, for the determination of 7 different cell types or development stages, a minimum of 26 spots of different marker genes are preferred, much preferred about 200 such spots. For full information, at least one spot for each of the presently 467 genes (markers) is preferred. A reduction of spot number can be of relevance e.g. if under certain conditions only a small subset of those genes listed in Tab II is required for analysis e.g. in clinical applications. This down compression can be achieved by determining the ratio of actual to target number of genes and then choosing from each cluster accordingly to the determined ratio the necessary number of genes to fulfill the requirement. This process requires to group the number of genes for each analysis of e.g. Tab. I into representative cluster families from where representative genes can be selected. Such clusters families can be determined as shown in Figure 1, namely by grouping clusters together that show a similar expression pattern. For each cluster family a representative number of genes may be chosen according to the compression factor that has been defined. It can easily be seen that for larger clusters like e.g. "A" in Tab I more genes are available to select while in other clusters like e.g. "E" in Tab I less are present. At the end of the process one needs to balance the procedure in order to preserve the characteristics of the expression profile. In order to do so the amount of genes for each analysis should at least be greater than 2 sequences or spots, respectively, of different genes and for the total array at least 30. In order to control such a process classical hierarchical clustering (Stanford) analysis can be performed and checked on graphical presentations like treeview (Stanford). Cluster analysis may group similar expression profiles in families and will allow distinguishing between different cell sources and allows classification of these cell cultures (see Fig. 2). If the cell sources are not properly represented in the cluster analysis it means that the selected marker genes are not balanced.

**Example of an cartilage specific micro array structure:**

To produce a microarray with printed oligonucleotides sequences of approx. at least 10 mers, preferably at least 25 mers, some sequences of table II need to be further processed. Since some of the  
5 determined sequences in Tab II are only expressed sequence tags (herein referred to as EST), they do not correspond to or represent the full-length cDNA. Therefore the EST preferably is BLAST searched with the public database at NCBI and the corresponding full-length cDNA determined. Only by having the correct and full-length cDNA it is possible to design  
10 oligomeric sequences that are balanced to each other and minimize any cross reactivity. Exemplary polynucleotide sequences (targets) are provided in the sequence listing of Table III. The cartilage related polynucleotide sequences as e.g. listed in Table III and other polynucleotide sequences known as key cartilage genes from the literature can be immobilized on a  
15 substrate and used as hybridizable array elements in a microarray format. Such microarrays can be composed of a subset of oligonucleotides representing e.g. sequences listed on Tab. II but modified to represent only full-length cDNA sequences. The used polynucleotides for the production of such a microarray can either be 50mer or also PCR (polymerase chain  
20 reaction) products but at least need to be longer than 10 bases. It should be noted that for microarray production also PCR products from the corresponding determined sequences directly or the full length cDNA can be used and it is not restricted just to oligonucleotides.

Methods to anchor such oligonucleotides or polynucleotides  
25 on a solid support are described in literature, together with information on length dependent distances between each oligo or polynucleotides and spots . (see e.g. Principal and Practice, DNA microarrays: gene expression analysis B.Jordan, Springer, 2001)

When polynucleotides are employed as hybridizable array  
30 elements in a microarray and depending on the software used, the array elements may be organized in an ordered fashion so that each element is present at a specified location on the substrate. If the array elements are at specified locations on the substrate, the hybridization patterns and

intensities (which together create a unique expression profile) can be interpreted in terms of expression levels of particular genes. This expression profile can then be used and may be correlated with any effect associated with a tissue and/or compound or to be investigated with regard to a specific tissue and/or compound and allows comparison with already existing data.

One of such useful application of using ordered polynucleotides on microarrays is e.g. the comparison of gene expression profiles from a new sample e.g. a tissue biopsy, with already determined characteristic gene expression profiles that are preferably stored in a database. Such stored gene expression profiles are e.g. of major importance if microarrays are applied in the clinic. In this case advantageously a database is set up that stores the corresponding gene expression profiles and advantageously also all patient informations, e.g. history, blood pressure etc. By including all patient data and gene expression profiles in the analysis process and then starting a comparison with an expression profile from a new biopsy, it becomes possible to achieve a stronger correlation with the clinical outcome. This will allow to determine which therapy shall be applied, or even to modify an existing therapy, e.g. to add growth factor x at a concentration y during the *ex vivo* tissue engineering phase. It may also be the case that the biopsy sample will demonstrate a poor gene expression profile that precludes the successful application of a modern therapeutic cell/tissue approach. Such cases would then only qualify for traditional surgical approaches, and hence would not obtain the benefits of the tissue engineering process.

In analogy, the assessment of *in vitro* produced cartilage can also be performed. In the same way as mentioned above cell culture parameters, like e.g. culture media conditions, growth factor concentration, are preferably stored in a data base together with the corresponding gene expression profiles. Comparison of the database entry with new profiles of new samples can then be used to assess the quality of the new *in vitro* produced tissue.



### Subject Arrays and their use:

It should be noted that the invention described here is not dependent on any special array format rather than the possibility to select from an extended list of 467 novel key cartilage genes as well as meaningful gene expression patterns. A presently preferred subject array is a novel cartilage specific microarray that includes 187 genes that in the scope of this invention have been determined to be cartilage related and 140 genes that have been connected to cartilage in literature (see also Tab III). Normally, in high-density array procedures up to 10000 genes are usually applied and are not specific for certain applications. As one major general drawback, this results in massive data overflow and impaired data analysis due to difficult data handling and procedures. A preferred array has in its current state a minimal number of 150 genes, presently much preferred at most 333 genes, all of those with demonstrated relevance within cartilage tissue. Another major limitation has become apparent. While the invention WO01/24833 A2 describes a few marker genes associated with cartilage phenotype stability they do not allow to extensively describe chondrocyte cultures in details. No comprehensive classification of the different cell populations and culture conditions is possible as well as no gene expression profile or fingerprint can be achieved. Gene expression profiles determined with a set of genes represented in Tab II may allow to perform a more comprehensive analysis of different cell cultures conditions. Furthermore it may allow to compare and classify different tissue or the result of the different applied cell culture conditions. The above mentioned topics may only be possible with the disclosed invention as outlined within the following applications.

The inventive array CART-CHIP 300™ may be applied to classify (quality control) any source material, such as human cartilage biopsies, mesenchymal stem cell containing bone marrow aspirate, or pre-chondrogenic cells containing tissue according to pre-defined categories with respect to their capacity to re-build or re-organize a hyaline cartilage-like matrix *in vitro*. A rough subdivision could be for example "A", "B", or "C". While "A" will easily produce cartilage-like matrix, "B" will require special treatment to achieve an implantable construct, and "C" will represent those

cases that do yet not qualify for such a procedure. This biopsy classification system will allow:

- Quality control of the starting biopsy material and therefore optimization of the downstream process regarding e.g. *in vitro* tissue engineering applications

- Diagnostic evaluation of the patient and candidate treatment methods (e.g. CARTIGRAFT™) to ensure a cost-optimized procedure

- Quality control of *in vitro* tissue engineered products

The subject array of the present invention can be employed for all kind of research and developmental studies related to *in vitro* tissue engineering of cartilage. The possibility to assess proliferation, differentiation or re-differentiation as well as de novo matrix formation processes through analyses and comparison of a plurality of key cartilage genes (positive/negative markers) within one single experiment replaces current trial and error approaches and is thus far more rational.

The subject array can be applied to screen all kind of drugs, e.g. hormones, growth factors, within *in vitro* chondrocyte cultures regarding a potential beneficial effect on proliferation, differentiation, de novo matrix formation. The deduced expression profiles can then be compared with existing data of e.g. native cartilage tissue and used to further optimize the process. Additionally the expression profiles can be compared with data from human adult and human infant cartilage to deduce a pathway or a strategy of how to induce more tissue formation *in vitro*.

The subject array of the preferred embodiment is very well suitable to better understand reaction pathways leading to new responses of chondrocytes *in vitro*. Only key cartilage genes comprising the whole spectrum of functional gene categories are to be investigated. This can be used to study the complexity of degenerative cartilage process *in vitro* and the respective influence of potential beneficial drugs.

The subject array may be used to optimize cultures for *in vitro* cartilage formation starting from human cell sources other than cartilage like e.g. mesenchymal stem cells or bon marrow aspirates.

This subject array will be preferably used as powerful alternative for conventional molecular biology tools beside more established histological and biochemical analyses. By focusing on the most prominent cartilage marker genes being either positive or negative, it is possible to characterize cartilage or cartilage related tissues as well as cell cultures thereof. In this respect, the subject array can replace conventional RT-PCR studies performed to check for cartilage marker gene expression, e.g. collagen I versus collagen II, aggrecan versus versican. By applying this subject array the set of markers will be easily increased by simultaneously simplifying the experimental procedure and enhancing the outcome.

The subject arrays of the present invention have several advantages compared to existing microarrays as well as to conventional gene expression tools such as RT-PCR, Northern Blots etc.

Most importantly, the subject arrays are all based on key cartilage genes. Beyond all the key cartilage genes known from the literature (~100-200 genes), 467 additional cartilage relevant genes have been discovered. Thus a significantly increased pool of cartilage key genes exists to choose from for various applications. For instance, to understand degenerative processes as they occur in OA or RA by study of complex biological reaction pathways, it is important to follow expression of a relatively large number of genes.

### Examples

The examples are described for the purposes of illustration and are not intended to limit the scope of the invention.

#### Example 1: Analysis of various human cartilage samples

Useful for characterizing chondrocyte cultures derived from different human cartilage samples (adult and fetal), where adult samples are different with respect to their capacity to form living tissue engineered equivalents under high density culture conditions.

Adult chondrocytes show different gene expression clusters compared to fetal chondrocytes and can be further distinguished from samples that will not produce living cartilage constructs (failures).

Human chondrocytes from adult and fetal articular cartilage  
5 were proliferated in DMEM-F12 medium containing 10% FCS over several passages and transferred to pellet cultures ( $0.5 \times 10^6$  cells) in serum free DMEM-F12 medium supplemented with Ascorbate and Insulin medium. Proliferated cells were directly lysed with RLT buffer (RNeasy<sup>®</sup> Mini Kit, Qiagen) after trypsin release from plastic substrate, shredded  
10 (QIAshredder, Qiagen) and kept frozen at  $-80^{\circ}\text{C}$  in lysis buffer for later processing. High density pellet cultures were cultivated for 2 weeks if not otherwise specified, subsequently washed with phosphate buffered saline (PBS) and lysed in RLT Buffer (supplied with RNeasy<sup>®</sup> Kit). Total RNA was isolated from all samples as described in the manual provided with the  
15 RNeasy kit and stored at  $-80^{\circ}\text{C}$ .

Fluorescent labeled aRNA (amplified RNA) constructs were obtained by *in vitro* reverse transcription of the RNA followed by an *in vitro* amplification reaction.

20

2  $\mu\text{g}$  of isolated total RNA were used per sample to amplify RNA by applying only one cycle of *in vitro* transcription (IVT, Millenium Biologix AG, Application Note).

25

2  $\mu\text{g}$  of total RNA from each sample was primed with oligo(dT)<sub>24-mer</sub> (containing a T7 RNA Polymerase Promotor) and reverse transcribed using 400 Units SuperScript II reverse transcriptase enzyme, nucleotides, 5x Reaction Buffer and Dithiothreitol (DTT) as described in protocol provided with the enzyme. For ribonuclease protection 1  $\mu\text{L}$  RNase inhibitor (10 Units) was used to prevent RNA degradation during first strand synthesis. This first  
30 strand synthesis reaction was incubated for 1 hour at  $42^{\circ}\text{C}$ .

To the first strand synthesis reaction 93 µl nuclease free water, 30 µl second strand buffer (Invitrogen, Basel, Switzerland) and 1.5 µl nucleotide mix (dATP, dTTP, dGTP, dCTP, 25 mM each) was added.

Second strand synthesis reaction mix was obtained by adding 40 Units E. coli polymerase I (New England Biolabs, BioConcept, Allschwil, Switzerland), 10 Units E. coli DNA Ligase (New England Biolabs, BioConcept, Allschwil, Switzerland) and 2.5 Units Ribonuclease H (Fermentas, Labforce AG, Nunningen, Switzerland). Reaction was incubated for 2 hours at 16°C.

After this incubation step remaining RNA was degraded by adding 7.5 µl 1M sodium hydroxid containing 2mM EDTA (Ethylenediaminetetraacetic acid) for 10 minutes at 65°C. 7.5 µl 1M Hydrochloric acid was added to neutralize the reaction.

The obtained double strand DNA was purified in a QIAquick® PCR purification kit (Qiagen, Hilden, Germany) and concentrated to 7.5 µl. To this concentrated RNA following reagents were added to obtain aRNA synthesis mix: 2 µl ATP (Adenosine triphosphate, 75mM), 2 µl GTP (Cytidin triphosphate, 75mM), 2 µl GTP (Guanosin triphosphate, 75mM), 2 µl UTP (Uridin triphosphate, 75mM), 1.5 µl 5-(3-aminoallyl)-Uridin triphosphate and 2 µl reaction buffer and 2 µl Enzyme mix (both provided with Ambion MegaScript Kit, Ambion, Cambridgeshire, United Kingdom).

This aRNA synthesis mix was incubated for 4 hours at 37°C. Remaining double strand DNA was digested by adding 1 µl Dnase I for 15 min at 37°C. aRNA was cleaned and concentrated with an RNeasy® Mini Kit column (Qiagen, Hilden Germany) and then concentrated to a final volume of 9 µl.

Fluorescent dye molecules were coupled to the reactive aminoallyl groups of the incorporated a 5-(3-aminoallyl)-Uridin triphosphate molecules. One aliquot of either Cy3™- or Cy5™-mono reactive dye (Amersham Biosciences, Buckinghamshire, United Kingdom) was diluted in 40 µl water free Dimethyl sulfoxide. 10 µl of one of the diluted Cy™ mono reactive dyes was added to each sample buffered in 100mM Carbonate

buffer (pH 9.00). Reaction was quenched after 1 hour by adding 10.4 µl Ethanol amine for 15 min at room temperature.

Unincorporated dye molecules were removed by ethanol precipitation. 2 µl Glycogen (Invitrogen, Basel, Switzerland) was added as carrier during precipitation. After precipitation aRNA pellet was washed with 80% ethanol, dried and resuspended in 50 µl 1x Fragmentation buffer (200mM Tris(hydroxymethyl)aminomethane hydrochloride, 500 mM Potassium acetate, 150mM Magnesium acetate). aRNA was fragmented for 35 min at 94°C and placed on ice immediately. Fragmented aRNA was dissolved in 900 µl hybridization buffer.

For denaturation aRNA was incubated for 5 min at 98°C and centrifuged for 30 sec at full speed in a microcentrifuge.

One CART-CHIP™ 300 (Millenium Biologix AG, Switzerland) was placed face down in a standard hybridization chamber. Hybridization solution containing the denatured and labeled aRNA sample was injected using a standard micropipet whereas Cy3™ and Cy5™ samples were hybridized together in one hybridization chamber (Millenium Biologix AG, Switzerland). The microarrays were incubated overnight at 42°C in a PCR thermal cycler (TGradient, Whatman Biometra GmbH, Göttingen, Germany).

After incubation unspecific aRNA probe was washed away with 1xSSC, 0.1%SDS for 5 min at room temperature, followed by another wash step in 1x SSC, 0.1% SDS for 5 min and rinsed with 1xSSC without SDS for 1 minute to remove excessive SDS. 1xSSC was discarded. Remaining 1xSSC buffer on the slide surface was removed by centrifuge the slide for 2 min at 1500 x g.

The dried CART-CHIP™ 300 were then scanned using an Affymetrix 418 microarray scanner.

Expression level raw data for every spot was obtained with ImageQuaNT (Molecular Dynamics). Raw data was normalized by dividing every expression value by total expression value of all spots for every sample and filtered by setting all values below the 25 percentile to the value of this 25 percentile to remove noise (25 percentile threshold).

For each sample (e.g. de-differentiated and re-differentiated chondrocytes) a list of all measured genes was generated. This so called gene expression profile was then used for subsequent analyses.

Further data analysis was performed using either hierarchical clustering with cluster.exe (written by Michael Eisen, Stanford University) or Self Organizing Maps (SOM), such as GeneCluster developed by Whitehead Institute (Massachusetts Institute of Technology, MIT). The settings of the software were optimized until a reasonable number of clusters resulted that were able to represent the comparison thoroughly. In the following example the parameters were as following:

Basic parameters: SOM rows 6; SOM col:4; #epochs=3000; #seeds=1

Advanced parameters: initialization: random vectors; neighborhood: bubble; alpha l=2; alpha f=0.005; sigma l=3000; sigma f=2.

Fig 1 shows a typical result from a SOM analysis with the above mentioned basic parameters, whereas Fig 2 shows an example of a graphical presentation of a cluster analysis and viewed by the software treeview.

## Example 2: Quality Control and Human Cartilage Sample Classification

Useful to demonstrate how CART-CHIP™ 300 can be used to differentiate between diverse cell culture conditions, to distinguish different patients, to study the influence of 3D culture conditions and to serve as a quality control tool during any tissue engineering process.

Human chondrocytes isolated from 4 different donors were proliferated over one passage (P1) and then cultivated as high density pellets ( $0.5 \cdot 10^6$  cells) in 3D culture for 7 and 14 days. RNA samples were taken from proliferated as well as from 3D cultured cells resulting in totally 12 different samples as shown in Figure 8. RNA isolated from this samples was shredded in a QIAshredder (QIAGEN, Hilden, Germany), amplified, hybridized, washed and scanned as described in Example 1.

Data sets for all 12 samples were extracted and normalized as described in Example 1 to perform cluster and SOM analysis as noted below. Cluster analysis was performed using normalized data computed with GeneCluster.

5 Fig 3 shows a picture of such a cluster analysis for all 12 samples (#1-#12) consisting of 20 clusters (c0-c19)

Every cluster represents a typical gene expression pattern for all 12 samples indicated by a point, starting from sample #1 on the left hand side to sample #12 on the right hand side in every cluster. For  
10 example cluster c0 represents the expression level of 104 genes in all 12 samples in a given range indicated by the lines located above and below the computed points.

Another example for gene expression levels that behave similar for different culture conditions and donors are depicted in clusters  
15 c3, c4, c9 and c10. Meaning that every subset of the three donor specific points #1-#3, #4-#6, #7-#9, #10-#12 (see Tab V for detailed description) have gene clusters that behave similar in all analyzed samples.

An example of differently behaving genes is indicated in cluster c13, representing 10 genes that behave similar in donor #1 and #2  
20 but show a different gene expression patterns for donors #3 and #4.

More detailed analyses are shown in Fig 4, Fig 5, and Fig 6. The clusters produced in these figures clearly demonstrate differences as well as similarities in cell behavior for either t0, t7 or t14 days, respectively.

25 Another software algorithm that can be applied for analysis of large amounts of data coming from gene microarrays is called hierarchical cluster analysis, whereas genes and/or different conditions with similar behavior in gene expression are clustered together. All hierarchical cluster analyses were performed using Cluster software described in Eisen  
30 et al. (1998) PNAS 95:14863) and displayed using treeview.exe developed by same author.

Fig 7 shows such a cluster of selected genes for all 12 samples analyzed. Every square is representing one single gene



expression value. Different intensity means different expression levels. Dark squares are representing samples without any significant change in gene expression compare to the other samples or patients. Bright squares are indicating samples in which genes are up- or down-regulated relative to other samples analyzed. A so called cluster of genes is a group of genes that behave similar from one donor to the other donors.

Not only genes but also samples can be clustered together. These clusters are called similarity dendrograms, shown in the top part of Fig 7. These tree-like structures illustrates similarities in gene expression between different samples or donors. The closer a sample (#1...#12) is located to another sample in this dendrogram the more similar gene pattern they have.

Interestingly to see is that the seven samples located at the right side of the dendrogram (samples #1, #2, #5, #7, #8, #10 and #11) are clustered together. This samples are representing t0 and t7 conditions as described above (illustrated in Tab V), whereas a cluster of 4 samples in the middle of the dendrogram (samples #3, #6, #9 and #12) are representing only t14 samples. This means a microarray of the current invention is able to distinguish between de-differentiated, proliferated samples (t0 and t7) and re-differentiated samples in a later stage (t14).

An outlier represents sample #4 located at the most left side of Fig 7. which represents proliferated chondrocytes (t0) from donor 2 and could not clustered together with the remaining proliferated samples. Interestingly, this sample that it is not similar to all other proliferated samples (#1, #7 and #10) was impaired with its capacity to form cartilage tissue equivalents following expansion in 2D culture. The biochemical analysis revealed a lower amount of total collagen/DNA for this sample and immunohistochemistry with collagen II antibodies resulted in only weak staining for a collagen II.

### Example 3: Aortic Fibroblasts vs. Chondrocytes

Example to differentiate between expanded chondrocytes and aortic fibroblasts cultivated over 14 days in 3D settings.

5 A human aortic fibroblast cell source was proliferated and brought to 3D culture. RNA was isolated after 14 days of culture. Expression data analysis was performed as described in previous Examples 1 and 2 using CART-CHIP™ 300 microarray.

10 A hierarchical cluster analysis was performed as described in example 2. Samples representing 3D culture after 14 days (t14) were included in said data analysis (samples #3, # 6, # 9 and #12, see Tab V).

The result of the described analysis can be seen in Fig 8. The upper part of the figure shows a dendrogram as described in example 2. Aortic fibroblasts are not clustered together with human chondrocytes. The cluster shows a significantly different pattern compared to all other  
15 cultures.

Obviously a gene expression pattern of an aortic fibroblast cell source can be clearly separated from a gene expression pattern of human chondrocytes. A micorarray of the present invention is therefore not only able to study differences between different chondrocyte culture  
20 conditions but also to distinguish between cells isolated from different tissues.

### Example 4: Arthritic conditions vs. healthy conditions

Useful to distinguish between normal healthy chondrocyte  
25 behavior from cells resembling an arthritic phenotype. Interleukin-1 $\beta$  is known to play a central role in the inflammation and connective tissue destruction observed in both rheumatoid arthritis (RA) and osteoarthritis (OA). Stimulation of *in vitro* chondrocyte cultures with Interleukin-1 $\beta$  thus represents a simple experimental arthritis model.

30 The chondrocyte cell source from donor 4 (see Tab V) was proliferated over 3 passages and then cultivated as high-density pellet cultures ( $0.5 \cdot 10^6$  cells) for 16 hours and 7 days either in the absence or presence of Interleukin-1 $\beta$  (30 ng/mL). RNA was isolated from all samples,

hybridized to CART-CHIP™ 300 and expression profiles were generated as described in Example 1.

- 5 A hierarchical cluster analysis was performed as described in Example 1 and the dendrogram and a selection of the representative gene clusters are shown in Fig 9. This clearly shows that already a short stimulus of Interleukin-1 $\beta$  results in alteration of the chondrocyte phenotype with gene expression changes that can be distinguished from untreated normal chondrocyte cultures.
-

**Appendix****Table I**

Experiment and correlated gene expression analysis	Number of marker genes for each experiment (analysis)	experiment (analysis)
2D marker adult vs. fetal/infant	151	A
2D /3D adult vs. fetal/infant	96	B
3D marker failure	165	C
3D marker adult/fetal/infant	350	D
2D/3D marker adult	48	E
Time dependent failure marker	75	F
3D failure marker	41	G
Apoptosis related failure markers	30	H

5

**Table V**

<b>Sample Numbers (#)</b>			
	<b>Proliferation (t0)</b>	<b>7 days in 3D culture (t7)</b>	<b>14 days in 3D culture (t14)</b>
<b>Donor 1</b>	<b>#1</b>	<b>#2</b>	<b>#3</b>
<b>Donor 2</b>	<b>#4</b>	<b>#5</b>	<b>#6</b>
<b>Donor 3</b>	<b>#7</b>	<b>#8</b>	<b>#9</b>
<b>Donor 4</b>	<b>#10</b>	<b>#11</b>	<b>#12</b>

10

**Table IV shows the results of a bioinformatic analysis of gene expression profiles of the 467 cartilage specific marker genes.**

Cluster	Accession	SOM Description	H4 P2 3D	H4 P2 2D	H4 P1 2D	H5 P1 3D	H5 P1 2D	H1 V2 10	H1 V2 2d	H1 V2 1d	H2 P1 3D	H2 P1 2D	H3 P4 10d	H3 F4 12d	H3 F4 12d	H3 F4 12d
2	AA283593	failure pool	0.558012600	0.48742855	0.602962907	0.97188478	3.50E-02	7.00E-02	0.32230383	0.4717391374	0.257739789	0.145513725	0.18755089	0.18755089	0.18755089	0.18755089
22	AA434158	2	1.822887384	2.058241156	1.793509407	2.19619189	1.28342518	1.683140939	1.384248400	1.041642418	1.859400003	1.335658822	1.018750369	1.018750369	1.018750369	1.018750369
22	RS2548	24	9.474062319	38.102234471	38.12885551	38.7272848	23.2884338	19.34185003	19.34185003	25.57074708	27.507195301	26.02420588	26.02420588	26.02420588	26.02420588	26.02420588
4	T07128	20/3D	0.159223543	0.239515222	0.111519832	0.115914938	0.104400087	0.104400087	0.104400087	0.104400087	0.104400087	0.104400087	0.104400087	0.104400087	0.104400087	0.104400087
8	AA845015	5	0.153365388	4.506017608	4.506017608	5.618102146	5.081143315	5.618102146	5.081143315	5.618102146	5.081143315	5.618102146	5.081143315	5.618102146	5.081143315	5.618102146
8	AA977895	20/3D	0.2355000155	3.523776419	2.904210444	2.88978265	0.897997266	0.457860281	0.897997266	0.457860281	0.897997266	0.457860281	0.897997266	0.457860281	0.897997266	0.457860281
15	AA844988	20/3D	0.135828438	12.95542024	10.58595044	11.734202081	11.734202081	11.734202081	11.734202081	11.734202081	11.734202081	11.734202081	11.734202081	11.734202081	11.734202081	11.734202081
16	AA844618	20/3D	34.85251230	39.31305252	38.10652307	32.87878549	64.75078549	64.75078549	64.75078549	64.75078549	64.75078549	64.75078549	64.75078549	64.75078549	64.75078549	64.75078549
16	AA845531	20/3D	66.81379424	89.14787581	89.14787581	89.14787581	89.14787581	89.14787581	89.14787581	89.14787581	89.14787581	89.14787581	89.14787581	89.14787581	89.14787581	89.14787581
20	AA847201	20/3D	54.4443367	59.1188028	59.1188028	64.7108842	64.7108842	64.7108842	64.7108842	64.7108842	64.7108842	64.7108842	64.7108842	64.7108842	64.7108842	64.7108842
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033
20	AA847201	20/3D	0.506029634	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033	0.810707033						



AA48200	2	3D oddit vs. fold	3.008242137	2.235002802	1.747620693	0.631226114	1.568028334	0.43393112	6.474436694	0.405348064	0.48291892	2.542018921	5.42E-02	7.67E-02	5.68E-02	0.744503100
H13691	19	3D oddit vs. fold	34.006273955	38.307049558	49.89794621	50.273732427	38.06839644	45.61749341	23.12024722	35.30376824	35.30376824	35.30376824	35.30376824	35.30376824	35.30376824	0.559497392
AA42036	3	3D oddit vs. fold	3.257550335	2.293125391	1.567514408	1.604761028	5.862999972	0.368363187	0.325060655	0.357001421	0.96974237	0.210123178	5.65E-02	0.197353989	0.197353989	1.83029539
AA46007	2	3D oddit vs. fold	4.351032023	4.44184644	1.452692862	1.418866207	5.709739731	0.513343664	0.342040973	1.411227879	0.464285516	1.167155762	0.4776998407	1.83029539	1.83029539	1.83029539
AA0495	2	3D oddit vs. fold	2.164560692	2.50168281	2.52095163	2.297385171	4.762374759	0.292201912	0.227321457	0.957785291	0.256506997	0.356529393	0.582450904	0.120562307	0.120562307	0.120562307
RS5709	2	3D oddit vs. fold	2.909306813	1.951341621	1.428889668	1.638106554	4.556456488	0.439230359	0.227321457	0.363274564	0.356529393	0.876E-02	2.14E-02	1.16E-02	0.672340722	0.672340722
H50114	2	3D oddit vs. fold	3.301713659	1.906391692	1.705940362	1.407414465	1.181045658	0.49230359	0.114292742	0.542003448	0.491910931	5.55E-02	1.78E-02	1.81E-02	0.120562307	0.120562307
AA4452041	2	3D oddit vs. fold	3.881943611	1.231373773	1.0248198	0.96393432	1.620394153	4.505593509	0.241515568	0.33997054	0.216285925	0.325697528	0.6686162	0.241219124	0.140120593	0.140120593
W73700	2	3D oddit vs. fold	3.914886357	1.697625973	1.679259731	1.608715372	2.2530904809	4.790266687	0.234847589	0.215971625	0.466556863	0.327233291	0.849E-02	0.104656358	0.735173064	0.735173064
N32002	17	3D oddit vs. fold	14.338225503	20.17733457	18.72682072	18.63895894	16.82011639	16.82011639	16.82011639	16.82011639	16.82011639	16.82011639	16.82011639	16.82011639	16.82011639	16.82011639
AA42915556	2	3D oddit vs. fold	6.164341067	2.312894111	1.624968319	1.595001607	5.460005928	0.384832268	0.205779688	0.205779688	0.205779688	0.205779688	0.205779688	0.205779688	0.205779688	0.205779688
AA4699510	2	3D oddit vs. fold	2.693239375	1.91870708	1.446745887	1.852271802	6.166238653	3.61E-02	0.12016161	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555
AA453787	2	3D oddit vs. fold	1.820556687	1.71735506	1.49078329	1.52261502	4.378025952	0.12016161	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555
H05555	2	3D oddit vs. fold	2.621892845	1.311605373	1.314199879	1.633779252	6.80770628	0.12016161	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555	0.515255555
AA4419177	2	3D oddit vs. fold	3.107515398	2.43742352	15.45485539	25.86215965	17.42786252	1.423422221	1.617002106	1.763710423	4.94920887	0.381612925	0.64E-04	0.46E-04	0.46E-04	0.46E-04
AA4458007	18	3D oddit vs. fold	18.65443357	25.43710014	28.20025412	20.47309658	38.78861672	38.78861672	38.78861672	38.78861672	38.78861672	38.78861672	38.78861672	38.78861672	38.78861672	38.78861672
AA4458007	18	3D oddit vs. fold	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6
W4660	17	3D oddit vs. fold	12.740951	10.68877	10.68877	10.68877	10.68877	10.68877	10.68877	10.68877	10.68877	10.68877	10.68877	10.68877	10.68877	10.68877
AA4620082	17	3D oddit vs. fold	14.5967618	11.53376895	14.7122923	14.7122923	14.7122923	14.7122923	14.7122923	14.7122923	14.7122923	14.7122923	14.7122923	14.7122923	14.7122923	14.7122923
TS2484	2	3D oddit vs. fold	3.293689407	3.026511181	1.69920999	1.69920999	1.69920999	1.69920999	1.69920999	1.69920999	1.69920999	1.69920999	1.69920999	1.69920999	1.69920999	1.69920999
AA4469910	2	3D oddit vs. fold	2.802422463	1.595897935	1.728521373	1.455020012	1.7234132	4.87783042	0.34E-02	0.712E-02	1.6895448	1.53377804	0.356012024	0.203021316	0.15693718	0.108397595
AA4468233	2	3D oddit vs. fold	1.05294328	3.81382356	2.016514163	1.40767353	1.46017865	0.340610827	0.819026283	0.619026283	0.808917	0.490260838	0.296042716	0.1168949	0.10547867	0.780074053
AA078775	2	3D oddit vs. fold	3.6041297	2.7056737	3.00955265	1.40767353	1.46017865	0.340610827	0.819026283	0.619026283	0.808917	0.490260838	0.296042716	0.1168949	0.10547867	0.780074053
W73889	2	3D oddit vs. fold	3.174704174	4.229312305	3.583500044	3.630704149	9.233162734	0.67326987	0.12612783	0.64173358	2.015290373	0.91813122	0.81E-02	0.13068981	0.581E-02	1.214742461
RS5337	2	3D oddit vs. fold	2.82398181	1.301117771	1.89060803	1.240681305	1.39156746	3.84378734	2.97E-02	2.35E-02	0.295841965	0.132909557	2.04E-02	-3.11E-05	1.07E-02	0.39363748
RS5049	2	3D oddit vs. fold	4.604550001	4.404550001	4.747834688	6.310431207	6.155225686	4.29201609	1.7177976	3.583304812	1.420346987	1.37128032	2.265029254	0.239935087	4.354026018	3.943026018
RA6321	2	3D oddit vs. fold	4.481781593	3.80517107	3.184315853	3.789730328	4.05931528	3.62974894	2.400280379	2.77656441	1.28136933	1.13735992	0.239935087	4.354026018	3.943026018	4.379816537
RS7853	2	3D oddit vs. fold	4.439371289	1.730958085	2.016576359	1.594216255	2.167157105	4.929747178	0.18976244	0.108548764	0.945269893	0.81E-02	0.13068981	0.581E-02	1.214742461	1.214742461
H69553	2	3D oddit vs. fold	3.47201163	3.16812583	3.07075883	1.873350025	2.52970287	6.529732134	0.13040047	0.105478654	0.236746317	0.351564341	0.45922235	3.87E-02	0.781599712	0.781599712
RS5346	2	3D oddit vs. fold	2.875024039	12.02169337	3.65642326	3.134285568	2.862300878	6.55744535	2.76509859	2.96566622	10.509634	1.628235254	1.778842428	1.69343824	1.550682609	3.471465224
AA422705	2	3D oddit vs. fold	6.763818698	1.673818698	1.673818698	1.673818698	1.673818698	1.673818698	1.673818698	1.673818698	1.673818698	1.673818698	1.673818698	1.673818698	1.673818698	1.673818698
AA487571	2	3D oddit vs. fold	2.392095741	2.030046374	1.893301674	1.445241912	3.841969377	0.118245357	0.10081175	0.118245357	0.426100265	0.110115471	3.86E-02	0.02671588	1.293134938	1.293134938
AA402440	2	3D oddit vs. fold	4.357574439	2.916837278	2.916837278	2.916837278	2.916837278	2.916837278	2.916837278	2.916837278	2.916837278	2.916837278	2.916837278	2.916837278	2.916837278	2.916837278
H28521	2	3D oddit vs. fold	3.458076591	2.080084868	1.72877255	1.459446529	1.929881092	2.32821042	0.20282398	0.454163231	1.143777395	0.607411285	0.90E-02	1.39247414	0.90E-02	1.2521297
AA469911	15	3D oddit vs. fold	28.62693085	28.62693085	28.62693085	28.62693085	28.62693085	28.62693085	28.62693085	28.62693085	28.62693085	28.62693085	28.62693085	28.62693085	28.62693085	28.62693085
AA468061	13	3D oddit vs. fold	10.41727699	8.937894327	15.0540142	10.40205372	10.40205372	10.40205372	10.40205372	10.40205372	10.40205372	10.40205372	10.40205372	10.40205372	10.40205372	10.40205372
AA448608	17	3D oddit vs. fold	14.1293138	11.54070062	18.075708	17.8394394	13.73538722	48.1549231	23.157253	22.55169347	18.4529368	20.5765682	20.5765682	20.5765682	20.5765682	20.5765682
AA467805	17	3D oddit vs. fold	11.02553598	9.596595949	16.74139733	14.13918278	13.48529484	10.63815359	27.4149216	22.05072859	23.33729443	27.50714539	22.7695523	27.50714539	27.50714539	27.50714539
RS755	18	3D oddit vs. fold	10.4122208	10.43470584	14.9705984	11.74181678	11.47500654	8.842282884	58.78281699	9.258281347	27.7763584	19.30516442	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	28.9345068	28.9345068	28.9345068
AA467955	18	3D oddit vs. fold	8.64740872	18.3745959	12.25345162	12.2140054	11.47500654	9.258281347	27.7763584	30.32716198	27.7763584	26.77163594	28.9345068	2		



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23	3D edit1 vs. fullure	0.861300108	6.204458487	1.365510688	0.568537573	0.970148717	1.578770394	0.384565828	0.43818572	0.422480014	0.236616384	1.181668077
R0876	3D edit1 vs. fullure	0.448119129	0.9484125705	1.349694388	0.122850054	7.01E-02	6.8E-02	1.742654009	0.150987638	0.158052088	0.251417300	
7	3D edit1 vs. fullure	3.948739465	2.28349781	2.994456379	6.00468275	0.213035184	0.818295152	0.462784956	0.177693697	0.237475848	1.13668202	
23	3D edit1 vs. fullure	4.970052897	3.285026099	3.5305944823	3.288338393	3.220959814	1.918198108	1.919736307	2.767598024	3.95242817	3.168886609	
49	3D edit1 vs. fullure	3.590147058	1.457265129	2.021263714	6.31631377	0.111757383	-3.0E-02	0.467435552	4.85E-02	1.52E-02	9.01E-03	
11	3D edit1 vs. fullure	1.3483519	1.56500104	2.531428853	0.18052753	0.180935388	0.84755028	0.256955028	0.098583152	0.01450502	0.41450502	
23	3D edit1 vs. fullure	3.826570897	1.93711377	1.77653592	16.32813848	1.330071481	8.778099249	9.71531194	0.180578833	1.277874076	0.674486801	
14	3D edit1 vs. fullure	2.174224052	45.10144344	2.069008838	1.31870518	0.127617118	0.173784942	0.65950467	0.22275821	2.79E-02	0.74486801	
14	3D edit1 vs. fullure	0.550596095	1.085306504	0.658682947	0.814517248	3.187258977	0.177514818	0.724810552	0.540552009	0.142613803	0.36898511	
N64882	3D edit1 vs. fullure	0.716578413	1.069480051	0.617778993	0.773891769	0.121761718	0.173784942	0.65950467	0.22275821	2.79E-02	0.74486801	
7	3D edit1 vs. fullure	4.173270074	6.098081459	5.192489359	6.808204083	17.32761828	18.58381924	9.4470581248	11.25375919	12.47382349	1.16820958	
R45413	3D edit1 vs. fullure	7.730845589	9.740301388	8.23360474	16.4589413	18.15909271	13.58205508	8.9470581248	11.25375919	12.47382349	1.16820958	
438187	3D edit1 vs. fullure	7.730845589	9.740301388	8.23360474	16.4589413	18.15909271	13.58205508	8.9470581248	11.25375919	12.47382349	1.16820958	
23	3D edit1 vs. fullure	23.09461759	12.79748882	19.87281182	25.31831892	19.5015243	30.08495758	24.1243143	28.19827013	36.68574593	36.36338944	
443834	3D edit1 vs. fullure	0.183674724	0.834546001	0.502237179	0.583081629	1.705238339	8.40E-02	0.248574669	0.115582005	2.84E-02	0.707338888	
23	3D edit1 vs. fullure	77.28842805	43.5841843	68.26595959	63.31937471	64.50243315	38.0529271	31.7882827	31.89233658	48.06811822	47.96403814	
7	3D edit1 vs. fullure	3.78957043	1.157647488	1.628208057	0.537045634	5.290408458	0.173802417	0.153440018	0.820011724	1.529093442	0.023894127	
7	3D edit1 vs. fullure	2.1516245668	76.64761828	1.455787277	1.89558391	22.68020328	0.247487714	0.188125893	0.227984638	5.912011779	0.223991418	
23	3D edit1 vs. fullure	0.78455272	18.90487628	1.124742532	2.680414555	4.298718254	0.088614529	8.03E-02	0.231928251	1.693504684	0.399206145	
11	3D edit1 vs. fullure	2.008155548	48.92472389	2.78974071	2.0174714	1.746871801	0.277245911	7.22E-02	6.894548016	0.117675022	0.155606077	
481758	3D edit1 vs. fullure	123.8211844	61.25063911	92.35920856	102.0348827	64.85370315	69.05370315	37.39817347	42.70517468	58.7187488	64.37630302	
321431	3D edit1 vs. fullure	125.2411904	93.8827224	64.85301063	61.83958518	47.8249648	55.38120705	77.3074377	76.1331828	8.41E-02	0.148593040	
4416103	3D edit1 vs. fullure	0.388824303	7.652704012	0.571045593	0.406838351	1.434683152	7.03E-02	1.215881727	1.077636559	0.757366523	42.06937518	
992646	3D edit1 vs. fullure	14.89709889	25.90172172	26.59330868	26.56872605	26.04183434	26.06764893	30.06204311	35.82818822	38.04822324	35.37693112	
453789	3D edit1 vs. fullure	2.1604150452	8.495598017	2.328028164	2.572187828	3.221697289	1.808400093	2.622494949	2.790194068	2.577690448	1.40223569	
432598	3D edit1 vs. fullure	7.087770078	9.918890598	7.937381894	7.650080272	8.794304531	7.329388134	13.08024669	14.28834182	18.54871153	18.674599	
8080929	3D edit1 vs. fullure	1.90911121	9.937986330	2.013089465	1.471073914	1.42828724	5.418655459	6.018942483	0.814412924	0.22361389	0.28581711	
R600119	3D edit1 vs. fullure	2.116044288	1.047607018	0.928042539	1.082721605	5.233772895	1.186841725	0.116811729	0.16841729	0.259384551	0.30049051	
48587343	3D edit1 vs. fullure	1.550037418	2.426871459	1.704823128	1.16868113	3.845429741	1.801017437	2.88976812	0.714779372	0.122688475	0.182166516	
18	3D edit1 vs. fullure	2.573932468	1.893217317	1.78341218	6.048739557	1.20178058	1.353486827	0.871366797	1.20764865	0.757366559	0.88002340	
18	3D edit1 vs. fullure	2.130783417	8.164653294	3.989770659	2.254035954	4.872785488	1.105347659	1.501678874	0.966552209	0.74069806	0.55317612	
798887	3D edit1 vs. fullure	1.100740146	1.501589727	7.015187496	1.820933972	3.33812636	2.356841611	0.312897784	0.312897784	0.401788982	0.938530357	
18	3D edit1 vs. fullure	3.703536587	1.841236581	0.469268355	1.570180807	8.384201758	0.287742527	0.229134882	0.372558688	1.777289392	0.041067898	
11	3D edit1 vs. fullure	4.911653574	2.905770718	6.153288807	3.258271808	3.421887145	1.884931477	3.005337914	3.005337914	3.005337914	3.005337914	
18	3D edit1 vs. fullure	1.342031068	1.952074132	3.34654568	1.625074182	4.341647063	0.389167344	0.389167344	0.389167344	0.389167344	0.389167344	
18	3D edit1 vs. fullure	2.862402028	7.4875271538	3.158373807	2.852355078	2.658007284	4.51872877	2.189019288	2.085757874	1.718808184	1.980668588	
18	3D edit1 vs. fullure	1.3595802693	7.059271875	2.232689884	1.921932585	1.953476223	0.414550187	0.201882284	0.21982789	0.751879444	0.125303880	
18	3D edit1 vs. fullure	2.032526698	8.058215003	2.287218034	2.287218034	2.287218034	2.287218034	2.287218034	2.287218034	2.287218034	2.287218034	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555	11.04039228	0.840304827	0.645047218	2.929147418	0.15138864	0.357518214	0.357518214	0.357518214	0.357518214	
18	3D edit1 vs. fullure	0.721995555										

H55958	3D	edit vs. failure	0.932240825	1.062851862	1.322524065	0.843203322	3.4263519	0.3427548	0.256922183	0.566515169	4.295907537	0.476155759	0.479105389	6.74E-02	1.020767749
AA458785	3D	edit vs. failure	1.02454481	1.073515465	1.016303139	1.117293959	3.608946499	0.795442166	1.506491022	0.808733277	1.828902108	0.920171532	0.659849251	0.690971385	1.994825669
AA485871	3D	edit vs. failure	1.240425485	1.019664978	1.051475658	1.243333278	4.885742561	0.597816889	1.768341753	0.134298619	2.137482817	0.626343105	0.254998284	0.126560593	1.303743017
T39411	3D	edit vs. failure	0.683415906	0.827762784	0.665695165	0.776303728	3.561109789	0.396231188	0.295018072	0.324545662	1.869345161	0.169337341	0.268104021	0.247903939	0.739491695
R00655	3D	edit vs. failure	1.45809863	2.768201659	2.659761885	2.788015121	1.087361074	1.087361074	1.02423951	0.766054262	0.953506121	0.535306121	0.154076211	0.154076211	0.154076211
H08666	3D	edit vs. failure	7.498281053	3.917399183	3.28047795	4.021330911	7.438138134	2.109762651	2.70484372	1.27574185	1.52882868	1.78402477	2.771446553	1.968370637	3.844030747
H72028	3D	edit vs. failure	1.122387248	1.077259289	0.894651185	0.936097551	5.4818260912	0.181183944	0.425147123	0.857472055	1.001641974	0.981420557	0.951793709	0.907756492	0.907756492
AA579177	3D	edit vs. failure	0.813501088	0.984726818	0.798756843	0.624866557	3.553140409	0.348135481	0.600333332	1.326863630	4.439877031	0.2930439	0.421386335	0.341502345	1.848279914
N21578	3D	edit vs. failure	0.492867681	0.650068088	0.332239214	0.43287101647	3.48974693	0.168101047	0.117603103	0.406969931	1.225918704	0.87E-02	2.22E-02	0.494287318	0.494287318
AA007419	3D	edit vs. failure	0.840548282	0.573707373	0.42558512	0.390973256	5.006931555	0.175402659	0.12813069	0.33815608	0.955234641	0.161989912	0.196276298	0.170532566	1.071232897
T48597	3D	edit vs. failure	1.478439588	1.061727019	1.085953458	1.158150178	3.878824078	0.398720468	0.670694257	0.403916103	1.234678181	0.125959577	3.27E-02	1.97E-02	1.338939338
N38559	3D	edit vs. failure	0.6566518	1.222440192	0.30241865	0.545373717	3.877892322	7.55E-02	1.055602220	7.313895545	2.658404237	0.307556568	0.724691759	0.970393719	1.035781305
R51912	3D	edit vs. failure	0.931665991	0.554068458	0.584770001	0.545373717	4.78485232	0.30759311	0.157062387	0.287430002	0.316950074	0.286956477	0.164570109	0.141668339	0.141668339
H04015	3D	edit vs. failure	1.027537339	1.409388868	1.543560847	1.015016188	0.913466897	0.339232734	1.16887454	8.324562689	1.997045708	0.350241169	0.100034162	0.78E-02	1.169187709
H41489	2D/3D	edit vs. faild	4.027393760	1.726349793	1.413362414	2.226316993	3.75946208	0.133063538	0.112846912	0.131903146	0.10540274	2.38E-02	2.54E-02	0.535589747	0.535589747
H15450	2D/3D	edit vs. faild	2.974647228	2.512436083	2.512436083	3.100940939	8.704786862	0.118493184	8.15E-02	0.870523766	0.121238973	9.91E-02	0.480360992	7.45E-02	0.480360992
W45416	2D/3D	edit vs. faild	1.053216881	2.6917705269	2.027050421	2.669737382	6.815095267	0.187478377	5.20E-02	0.722050962	0.692564761	0.293080465	0.169933558	7.45E-02	0.655830442
AA487751	2D/3D	edit vs. faild	3.707303465	2.223590687	2.427972778	2.531458169	7.623880101	0.7693974	0.76016922	0.528464235	1.211081639	0.239897162	0.171663979	0.272889223	0.103051393
AA487486	2D/3D	edit vs. faild	4.045765601	3.016232294	2.88502619	2.768946605	8.048478337	0.634940441	0.935010842	1.665390778	0.752825561	0.193793075	0.19174164	1.934118861	1.934118861
R66604	2D/3D	edit vs. faild	3.846779908	2.979815371	2.369299368	3.1598912	7.450689126	0.3460238	0.409195433	1.083709289	0.659089131	0.60487088	0.489048814	0.385606238	1.892178098
T57572	2D/3D	edit vs. faild	4.48763913	2.538266605	2.543615768	2.482140712	3.902866448	0.25838637	0.186483973	0.235991068	0.28337251	0.46888307	0.109303057	0.116658413	1.388384083
H15085	2D/3D	edit vs. faild	4.520779808	1.874728575	1.797826535	2.418235338	7.10815384	0.157568914	0.114768422	0.508468022	0.673401507	0.17751889	0.655E-02	5.08E-02	0.13800474
R91295	2D/3D	edit vs. faild	6.7522623	2.946120833	2.946120833	2.828103944	7.88061273	0.212945474	0.159171688	1.553133951	0.607242405	0.169255202	0.225692165	0.169255202	0.384976032
T61256	2D/3D	edit vs. faild	1.64166539	1.818566112	1.625856706	2.423048555	6.87837501	7.25E-02	0.151774276	0.78113947	1.452405528	0.84E-02	7.32E-02	0.145E-02	1.055956615
AA405731	2D/3D	edit vs. faild	34.42423868	1.844515989	1.304288082	1.923015338	0.6339388	0.195114784	0.139449531	0.39111259	3.35219508	0.15088395	0.199491769	0.012689025	0.012689025
T71879	2D/3D	edit vs. faild	4.193732889	1.924212663	1.946581372	1.956665508	8.143137484	0.129333321	0.13741443	0.350507778	0.407085628	0.14225993	4.49E-02	2.40E-02	0.521726093
H5927	2D/3D	edit vs. faild	4.876208077	4.383531971	1.923441449	1.5257404	2.192296827	7.95477286	8.10E-02	0.10739205	0.50E-02	0.44222621	9.27E-02	9.43E-02	0.347354052
AA495780	2D/3D	edit vs. faild	1.514704846	0.912628215	0.912628215	0.912628215	0.48080188	0.022487653	0.354583826	0.78488653	1.752767589	0.281892243	0.187224487	0.825E-02	1.131163315
AA176689	2D/3D	edit vs. faild	0.853913275	0.853913275	0.753970468	0.781878518	8.758214974	0.178382771	0.14456552	0.284863046	2.416941887	0.161950808	0.3988222	0.825E-02	0.550312165
AA439163	2D/3D	edit vs. faild	1.145288483	1.650591644	1.291875543	1.52645481	1.92855481	0.105802982	9.20E-02	0.284863046	2.416941887	0.161950808	0.3988222	0.825E-02	0.550312165
AA421878	2D/3D	edit vs. faild	1.93927997	0.91028893	0.91028893	0.91028893	0.91028893	0.91028893	0.91028893	0.91028893	0.91028893	0.91028893	0.91028893	0.91028893	0.91028893
AA452225	2D/3D	edit vs. faild	1.905476839	1.545220165	1.41603191	1.289593725	9.71220085	0.27222988	0.152997555	1.039475243	2.150330865	0.416397658	0.329192564	0.19424438	1.91291602
AA482426	2D/3D	edit vs. faild	25.87139954	1.69374278	1.69374278	1.69374278	9.859144828	0.28952741	0.373831514	0.418062991	1.681826031	0.191563224	0.121355580	1.268933317	1.268933317
V17485	2D/3D	edit vs. faild	1.745341956	1.287668441	1.305011988	1.16482719	11.04780889	0.29071332	0.50588816	0.290834133	1.405085787	0.21336319	0.172813844	2.02E-02	0.952779161
H84982	2D/3D	edit vs. faild	1.530328723	1.047589817	1.540633971	1.23868481	9.82918448	0.131638592	0.1757575218	2.013022257	9.62E-02	0.376525133	9.28E-02	0.503147875	0.503147875
AA504615	2D/3D	edit vs. faild	4.05025188	1.645750443	1.641384078	1.891688149	8.286429124	0.176887945	0.345860294	0.630918749	2.620578978	0.183460578	0.121344263	0.12161682	1.972320295
AA48859	2D/3D	edit vs. faild	3.124580125	3.89374795	3.45126359	3.45126359	6.73032821	2.916582897	2.830305992	1.637325243	13.34753362	0.26009453	0.180111066	0.132777558	2.0701127
AA07058	2D/3D	edit vs. faild	1.554102379	1.933530283	1.58498753	2.64239309	9.4800034	4.54E-02	4.13E-02	0.397054172	0.116749427	4.89E-02	2.03E-02	2.81E-02	0.24403144
AA453401	2D/3D	edit vs. faild	8.692934592	1.905653823	1.904350636	2.20453207	8.672888766	0.167663345	0.214807788	0.222222695	0.203904483	0.242997288	0.251569524	0.177121661	0.804208418
N66737	2D/3D	edit vs. faild	24.90073088	1.095420779	0.552806838	0.823755381	3.44204218	4.30E-02	7.41E-02	0.257268707	28.36551857	1.04810846	0.091475556	0.104092366	0.76476014
AA680180	2D/3D	edit vs. faild	12.05725753	2.1570443	1.488045473	1.0762054	5.343732485	3.198031019	7.187377922	29.1323485	10.64207727	2.781542964	3.996641952	4.04434302	4.66818378
AA857131	2D/3D	edit vs. faild	0.20746704	0.26097471	0.210685319	0.132387182	0.35740785	0.22573307	0.63E-02	0.763187241	23.03560077	0.07088238	3.60E-02	4.56E-02	0.978719343
AA479102	2D/3D	edit vs. faild	25.01625351	3.681214695	3.42592628	3.02851039	6.0811205	0.852940035	8.120715713	9.238793772	11.51815786	4.75393954	7.003983588	5.685548034	5.685548034
R87487	2D/3D	edit vs. faild	4.592291885	4.76163135	3.922665505	4.97668385	11.60187681	1.325946518	1.245447159	1.481089768	1.481089768	0.592776193	0.435487259	1.471236654	1.471236654
AA456077	2D/3D	edit vs. faild	7.731170292	7.55857203	7.55857203	7.55857203	7.55857203	7.55857203	7.55857203	7.55857203	7.55857203	7.55857203	7.55857203	7.55857203	7.55857203
R87487	2D/3D	edit vs. faild	7.12414318	3.928552441	3.587814728	3.928552441	10.82120885	0.771648813	0.859478249	0.801080192	1.362042481	0.429437896	0.408760893	1.063446988	1.063446988
AA406259	2D/3D	edit vs. faild	6.463700059	3.376570613	2.35908775	3.43790579	11.9086873	0.270855482	0.224555482	1.0680255	1.245798874	0.124210479	6.82E-02	9.79E-02	0.974778072
H474823	2D/3D	edit vs. faild	0.885522209	0.507568185	0.423927188	0.05894222	1.328758097	0.147625314	0.155574422	0.39193035	7.661750853	0.116891312	3.09E-02	3.09E-02	0.687478991
H69384	2D/3D	edit vs. faild	3.867846832	2.58202058	2.58202058	2.58202058	9.99531084	0.368774275	1.09104021	1.678071183	0.316922232	0.10853159	0.10216458	1.465520888	1.465520888
AA41684	2D/3D	edit vs. faild	14.43916872	4.76379151	2.471882235	2.78135077	8.78313934	0.497110821	0.537175623	0.625425472	1.45981244	4.89E-02	2.74E-02	5.04E-02	0.135203872
AA482301	2D/3D	edit vs. faild	2.638926534	3.116535142	3.116535142	3.116535142	8.08592684	0.69E-02	0.207178204	0.502532552	1.277477858	0.722330552	0.144466915	0.144466915	2.238318784
H09588	2D/3D	edit vs. faild	1.455459708	0.93818073	0.705683294	0.91408074	9.587415089	0.22776882	0.168033375	0.379322002	7.180982801	0.247795566	0.18794709	0.18794709	1.31

AA653271	5
AA606957	5
AA757764	2
AA406064	2
194596	20
AA481688	7
182394	3
120148	3
AA486878	3
AA400973	3
AA497027	3
NG4508	3
AA333564	3
AA446108	3
AA159577	3
R30958	3
AA629808	3
AA482087	3
AA669314	3
AA775241	3
R73584	3
H28984	5
R44202	3
W70051	4
AA401972	5
AA239104	5
R22412	5
AA424804	5
AA669443	5
R69689	2
H24316	4
AA077424	3
R30571	4
AA050465	4
AA633011	4
AA457185	4
AA459104	4
R40212	4
AA068478	4
AA693310	5
AA455040	1
AA496878	1
AA085748	1
AA425753	1
H52350	1
AA630104	1
AA454854	1
W73406	2
R12002	1
AA405355	2
AA482930	1
AA629189	1
AA430512	0
AA458439	0

0	2D Marker editd vs. fcdl	H27964	4.0830677399	3.2471077731	3.68259994	4.052835461	3.078145192	3.785715273	8.22114128	10.7972650	9.655471293	7.905744552	7.17124051
0	2D Marker editd vs. fcdl	A644057	2.74055753	3.282718575	2.77240442	2.635366393	2.303198312	14.7786764	17.4727252	14.48782372	14.68818169	8.969157428	8.969157428
0	2D Marker editd vs. fcdl	R0460	2.77040419	2.345748987	2.593126394	2.129550659	6.325597621	8.741493109	13.22626391	14.29766841	14.29766841	14.29766841	14.29766841
1	2D Marker editd vs. fcdl	W965058	0.551733053	0.623172885	0.847514864	0.847514864	0.847514864	8.316574842	5.802080978	9.091198422	6.943430065	7.898182293	6.501586694
2	2D Marker editd vs. fcdl	T72202	0.054777756	1.354165555	1.335263319	1.298146537	4.910001899	5.615500921	4.651309743	4.997121679	7.50542874	5.521261935	4.693558807
3	2D Marker editd vs. fcdl	A5369794	0.447901918	0.8992041	0.470408129	2.053941181	0.579341161	8.49402	0.244500877	0.307166755	7.77162	0.048932125	0.163149057
3	2D Marker editd vs. fcdl	A398178	1.076236657	3.616532931	3.4704198129	2.267545118	1.70047268	0.901932337	8.557632935	0.480744514	0.048932125	0.048932125	0.495252613
3	2D Marker editd vs. fcdl	R8247	4.145653904	3.807020517	3.2471659312	4.81159689	16.0853392	0.546118994	0.291419248	0.128481144	1.85E-02	0.7026699	0.425481979
3	2D Marker editd vs. fcdl	T98812	0.295559478	3.762388177	4.4639330265	4.4639330265	4.4639330265	0.291419248	0.128481144	0.128481144	0.128481144	0.128481144	0.128481144
3	2D Marker editd vs. fcdl	A4454658	0.357268094	3.908407295	1.39103569	0.223335364	0.266810127	0.174714807	0.035760373	0.103986394	3.71E-02	0.245353665	0.245353665
3	2D Marker editd vs. fcdl	N57604	1.330276894	3.770520181	3.257268094	3.908407295	1.39103569	0.223335364	0.266810127	0.174714807	0.035760373	0.103986394	0.245353665
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
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2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
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2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
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2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.16695328
2	2D Marker editd vs. fcdl	A7776875	0.237874789	0.30807128	0.2764005	0.30301513	10.1431863	7.592113989	4.34522558	3.951620223	4.536042504	6.665103937	7.

Y73892	19	2D Marker addit. va. total	53.02002013	39.02380555	38.30704959	58.03742629	53.02918111	48.25990911	20.27131765	22.07700187	17.82409994	12.42684249	13.03977038	19.26896493	19.76283359	12.52223224
Y73893	19	2D Marker addit. va. total	50.1355528	37.01865341	36.30704959	48.08353034	47.57514229	45.25023946	16.0676331	16.21613077	13.02265984	12.77803984	9.864335148	18.31280635	19.12043735	10.93049688
H57138	13	2D Marker addit. va. total	10.27189646	9.124487788	8.90585148	8.90585148	11.12523179	10.90992918	23.82835337	23.14775405	17.84717904	22.81317102	27.82013989	19.11366361	18.60407949	16.60407949
AA709414	23	2D Marker addit. va. total	72.81271834	37.61546462	36.30704959	69.87343991	62.22823659	64.44118419	28.71182323	30.84738122	28.5320194	35.02886478	37.03232417	37.03232417	23.51879387	23.51879387
AA438584	15	2D Marker addit. va. total	15.24754038	6.426887725	6.078129118	6.078129118	22.73911159	19.61483081	1.582316414	2.17042252	6.760578809	9.12471674	1.1524513	1.304988693	1.304988693	2.225501134
AA026042	9	2D Marker addit. va. total	8.022234644	7.311595005	8.99560277	9.478217739	9.605465934	7.544837481	23.54904697	23.54904697	18.01970787	20.5027043	24.29216348	10.0915921	7.199816962	5.465605703
AA42725	9	2D Marker addit. va. total	12.6924684	7.555538142	13.07326612	4.281155304	12.4200971	12.81248352	30.1691519	22.80525120	22.9553184	27.6782775	24.29216348	19.81070818	18.07220606	14.02068164
N51280	9	2D Marker addit. va. total	6.822333815	7.385185272	7.55098106	7.55098106	7.765748508	8.99350251	27.65225951	31.81602093	22.9553184	27.6782775	24.29216348	19.81070818	18.07220606	14.02068164
AA231347	8	2D Marker addit. va. total	5.088780813	4.80487592	4.81159344	8.45211025	8.288204512	4.89065004	22.81574164	25.60885154	14.8874075	18.071738	24.29216348	19.81070818	18.07220606	14.02068164
AA402860	8	2D Marker addit. va. total	4.955150821	4.50182224	6.586223621	7.556713599	8.476099122	4.89065004	22.81574164	25.60885154	14.8874075	18.071738	24.29216348	19.81070818	18.07220606	14.02068164
N94835	9	2D Marker addit. va. total	7.15049257	6.84112951	4.46705412	6.046321655	6.506092414	8.476099122	23.18377589	21.24725933	22.9553184	27.6782775	24.29216348	19.81070818	18.07220606	14.02068164
AA490209	7	2D Marker addit. va. total	5.893194729	5.824093	4.46705412	6.046321655	6.506092414	8.476099122	23.18377589	21.24725933	22.9553184	27.6782775	24.29216348	19.81070818	18.07220606	14.02068164
W61301	8	2D Marker addit. va. total	7.335288225	7.335288225	11.0935518	8.10000027	9.421701778	6.881790584	34.10378475	31.17781958	34.01829551	28.43189884	23.02878278	24.56402722	27.14137043	33.29284339
N51018	7	2D Marker addit. va. total	5.486100802	38.5282212	10.6993048	8.002534568	5.210842488	9.99599739	8.99599739	8.99599739	8.99599739	8.99599739	8.99599739	8.99599739	8.99599739	8.99599739
AA45281	7	2D Marker addit. va. total	9.317439818	8.095460011	8.095460011	7.528285088	7.938571107	8.10070507	5.842816598	5.842816598	3.409051258	2.155743141	3.214857053	0.48554727	0.500500102	3.973103928
W68471	7	2D Marker addit. va. total	7.215222787	8.14855458	8.14855458	5.32000885	4.95859017	13.58485747	2.178145049	2.282871009	1.89901302	4.280699971	3.214857053	5.781751821	8.1678428	6.99599739
AA46831	7	2D Marker addit. va. total	6.816843406	3.698421687	10.1148224	5.538922361	5.404778773	6.062778817	1.034914816	1.422816774	15.19820754	7.15723164	1.524710041	1.404545398	4.18059495	4.18059495
AA458982	7	2D Marker addit. va. total	6.96128658	6.289775268	8.441469774	7.07292475	7.54658009	6.402438243	5.030128946	5.671175844	3.252721767	3.668109484	2.80818532	4.18059495	3.95909691	3.95909691
AA44095	7	2D Marker addit. va. total	10.5388887	9.89251828	8.005104314	8.530732052	8.715924875	7.359807298	4.829174413	4.815478182	3.252721767	3.668109484	2.80818532	4.18059495	3.95909691	3.95909691
N99003	7	2D Marker addit. va. total	7.773784527	6.12340597	7.271350835	7.694076299	8.015058524	6.94784869	2.03962485	2.553557284	1.92061882	1.45678544	2.0821831	1.98535512	1.595312179	1.595312179
AA00284	7	2D Marker addit. va. total	6.816843406	3.698421687	10.1148224	5.538922361	5.404778773	6.062778817	1.034914816	1.422816774	15.19820754	7.15723164	1.524710041	1.404545398	4.18059495	4.18059495
AA195308	12	2D Marker addit. va. total	4.730231812	5.630223489	6.168418227	3.952137125	6.29183958	3.139371467	22.51612405	19.8134058	1.19451555	1.284845386	2.17588501	1.85888897	1.575172599	3.007724228
AA478268	8	2D Marker addit. va. total	4.597623085	4.31865821	6.0746738	5.201094819	6.70579389	4.273131809	11.98015041	10.9922076	22.51612405	19.8134058	1.19451555	1.284845386	2.17588501	1.85888897
AA00583	13	2D Marker addit. va. total	8.710213419	6.83931914	10.89287008	9.897803204	10.76405811	7.534384828	28.6604723	25.63350529	30.51834358	30.51834358	30.51834358	30.51834358	30.51834358	20.25522038
AA461435	13	2D Marker addit. va. total	10.8653107	8.87839398	11.7070231	9.862860468	10.62008087	10.8053389	21.82366331	20.08886964	18.86282313	22.61456637	25.53193188	21.93073816	21.93073816	13.12038825
AA05049	13	2D Marker addit. va. total	7.774740452	7.086628819	10.84932581	7.697584813	7.63232488	5.43221512	22.0904745	23.18389428	18.86282313	22.61456637	25.53193188	21.93073816	21.93073816	13.12038825
AA487893	13	2D Marker addit. va. total	8.397913167	8.09379167	10.38317053	8.186637919	8.67781639	6.54527414	19.6188578	19.6188578	17.2329505	24.0071361	26.53431361	17.75512522	25.91589988	13.62120963
AA22220	12	2D Marker addit. va. total	8.978311755	8.408379167	9.99957753	8.245173408	8.4533271	7.94255354	48.60821655	42.38507553	23.18186775	28.16377551	30.53228609	41.74842514	54.37488138	30.13431188
H87108	9	2D Marker addit. va. total	8.511773188	8.09765668	8.83928411	6.88270747	9.81788232	7.40551924	20.83881132	14.25930268	17.92470533	21.26931436	23.8829193	22.7822035	22.7822035	16.76789738
W68480	12	2D Marker addit. va. total	6.333304604	6.11454874	10.3854816	8.28505538	8.50184885	6.781830425	23.07654727	21.55396893	24.06895954	28.16647168	31.37132599	30.73988527	31.10877394	17.78020978
AA405800	12	2D Marker addit. va. total	6.12197759	7.721500548	7.721500548	10.92459784	13.45540044	19.8931482	28.38840187	25.78862125	25.65907432	25.93028811	29.14739213	20.1376127	20.1376127	15.43920589
TS1539	12	2D Marker addit. va. total	8.489000148	8.10525851	8.48900097	8.82024288	9.40419114	5.893142749	37.04254749	35.58328862	27.22357679	29.39443068	29.26747712	32.85179948	37.13241221	24.37523888
N59164	12	2D Marker addit. va. total	7.600540659	4.756724822	8.39191538	7.27890425	6.135204655	6.251234677	24.33005591	22.53923003	18.07456069	26.90427659	20.92597239	20.92597239	20.92597239	16.44003019
AA521348	11	2D Marker addit. va. total	18.0187463	11.98813991	20.04539147	17.86437255	19.7279582	15.4466558	3.927402453	4.183573541	4.871008917	6.00926354	4.22027818	6.41272638	6.63139483	4.36487316
AA42551	11	2D Marker addit. va. total	13.57795945	12.53971	13.57795945	12.53971	14.28115078	11.3187892	7.51121628	7.054388812	6.39066859	6.39784337	4.74719124	11.79753397	11.0853014	8.92439722
AA463383	11	2D Marker addit. va. total	6.40710185	6.40710185	10.63654528	8.115297349	8.34580882	8.5884507	3.95207402	4.363727488	3.62188978	3.881140008	6.05844423	6.05844423	6.05844423	8.92439722
AA450172	11	2D Marker addit. va. total	1.415297485	1.415297485	17.38715258	12.09048918	8.29046893	6.184780432	8.583846144	2.818134848	16.590439	4.55242258	5.08460046	5.08460046	5.08460046	8.75506895
AA50477	12	2D Marker addit. va. total	3.85972235	6.80353431	6.80353431	6.20924721	8.62042051	4.858915508	20.27058258	23.61171233	22.8431145	20.65453263	28.05909595	20.61037432	19.18150684	15.10222793



### Claims

1. A method for the identification of tissue/cell specific marker genes comprising

a) taking tissue and/or cells of at least one developmental stage and/or at least one disease state, and/or

cultivating said tissue and/or cells *in vitro* under at least one culture condition,

b) determination of gene expression profiles of said tissue/cells and/or *in vitro* cultivated tissue/cells and

c) identification of specific marker genes by bioinformatic analysis of said gene expression profiles.

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2. The method of claim 1 comprising cultivating tissue/cells of at least two different developmental stages and/or disease states *in vitro* under at least two different culture conditions, determination of gene expression profiles of said *in vitro* cultivated tissue/cells and identification of specific marker genes by bioinformatic analysis of said gene expression profiles.

3. The method of claim 1 or 2, wherein said tissue/cells are selected from the group consisting of fetal tissue, adolescent tissue, adult tissue, healthy tissue and pathological tissue, progenitor cells like stem cells or cells derived from the same precursor lineage.

4. The method of anyone of claims 1 to 3, wherein said culture conditions are 2D and 3D *in vitro* cultures.

5. The method of anyone of claims 1 to 4, wherein said gene expression profiles are determined by a micro-array.

6. The method of anyone of claims 1 to 5, wherein said bioinformatic analysis is done by software analysis like e.g. SOM or cluster analysis.

7. The method of anyone of claims 1 to 6 where the tissue is cartilage.

8. A method for the determination of a particular disease state or developmental status of cells/tissue or the physiological potential of

cells/tissue comprising establishing a gene expression profile of said cells or tissue, comparison of said resulting profile with profiles characteristic for a particular status or physiological potential of the examined cells/tissue and determination of the particular status of the examined tissue/cells.

9. The method of claim 8, wherein said profile is a gene expression profile which is determined by means of a micro-array.

10. The method of claim 8 or 9, wherein said tissue is cartilage tissue or chondrocytes, preferably derived from arthritic joint tissue (rheumatoid and osteoarthritis), and the micro-array comprises polynucleotide probes of tissue specific marker genes.

11. A method for the determination of characteristic gene expression profiles for clinical use comprising:

- a) determining gene expression profiles of tissue or cell samples *in vitro* and generating a database containing said gene expression profiles,
- b) correlating patient datas e.g. patient history, medication etc. of the tissue or cell sample donor with the gene expression profile of said tissue or cell samples and optionally the clinical outcome after treatment.

12. The method of claim 11, wherein said gene expression profile has been determined by a method of claims 8 to 10.

13. A cartilage array comprising a plurality of different polynucleotide probe spots stably associated with a solid surface of a carrier, whereby each of said spots is made of a unique polynucleotide that corresponds to one specific cartilage marker gene.

14. The cartilage array of claim 13 comprising at least two spots that have different nucleotide sequences but of the same cartilage marker gene.

15. The cartilage array of claims 13 or 14 comprising at least 10 spots of different nucleotide sequences and being indicative of a specific tissue or cell status.

16. The cartilage array of anyone of claims 13 to 15 comprising spots of different nucleotide sequences and that are indicative for at least two tissue or cell status, preferably 3 status.

17. The cartilage array of anyone of claims 13 to 16, wherein at least part of the cartilage marker genes is selected from the 467 genes listed in the description, preferably at least 10 %, more preferably at least 50 %, most preferably about 100 %.

18. The cartilage array of anyone of claims 13 to 17, wherein said different polynucleotides of the array do not cross hybridise under stringent conditions with each other.

19. The cartilage array of anyone of claims 13 to 18, wherein the status is selected from biopsies and/or 2D cultures and/or 3D cultures of healthy adult, healthy fetal/infant, undesired adult, undesired fetal/infant or progenitor cells like e.g. stem cell or cells derived from the same precursor lineage.

20. The cartilage array of anyone of claims 13 to 19, wherein the polynucleotide probes have a length of at least 10 nucleotides, preferably at least 25 nucleotides.

21. The cartilage array of anyone of claims 13 to 20, wherein the carrier is optionally attached to coated glass, nylon or any other material.

22. The cartilage array of anyone of claims 13 to 21, wherein at least part of the cartilage marker genes are selected from a subgroup of the 467 genes listed in the description, said subgroup consisting of the most tissue specific 200 genes.

23. The cartilage array of anyone of claims 13 to 22 which can be used within clinical applications as a diagnostic tool in order to assess patient biopsy/cell samples for targeted *in vitro* cell culture treatment/performance when performing a cell or tissue based therapy.

24. The cartilage array of anyone of claims 13 to 22 which can be used within clinical applications as a diagnostic tool in order to assess patient biopsy/cell samples and to decide on subsequent therapeutic approach which maybe a tissue engineered therapy, a cell therapy only, or even a traditional surgical approach only.



25. The cartilage array of anyone of claims 13 to 22 which can be used as a quality control tool in order to assess the quality of human biopsy/cell samples prior performing the cellular expansion in case of cell therapy and/or prior performing the differentiation/tissue formation in case of a tissue engineered therapy.

26. The cartilage array of anyone of claims 13 to 22 which can be used as a quality control tool in order to assess the quality of the final implant prior and/or after product release, said implant being proliferated cells in case of a cell therapy or tissue engineered cartilage in case of a tissue engineered therapeutic approach.

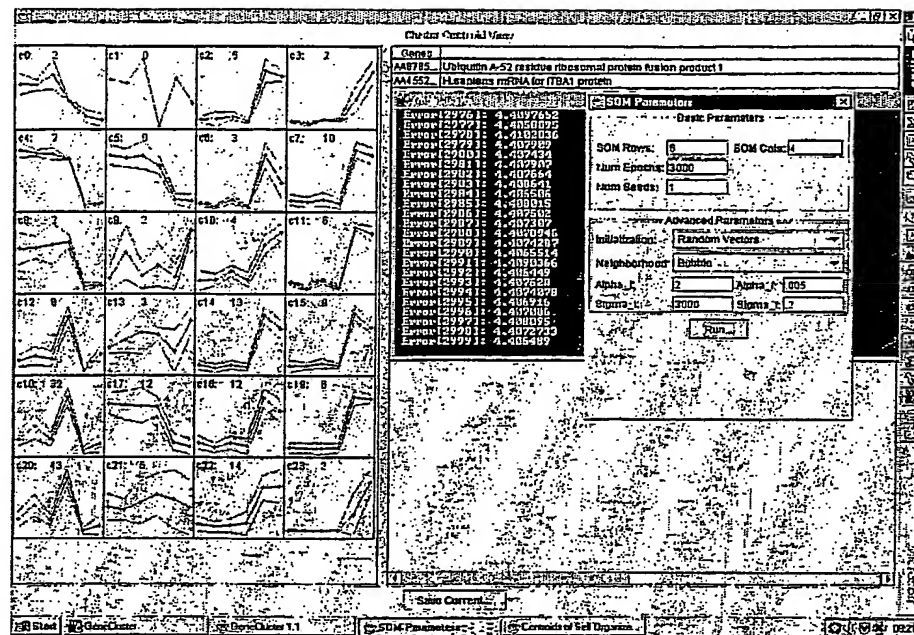
27. A kit for use in a hybridization assay comprising a cartilage array of anyone of claims 13 to 26.

28. The kit of claim 27, wherein said kit further comprises reagents for generating a labelled target polynucleotide sample, a hybridization buffer and a wash medium.

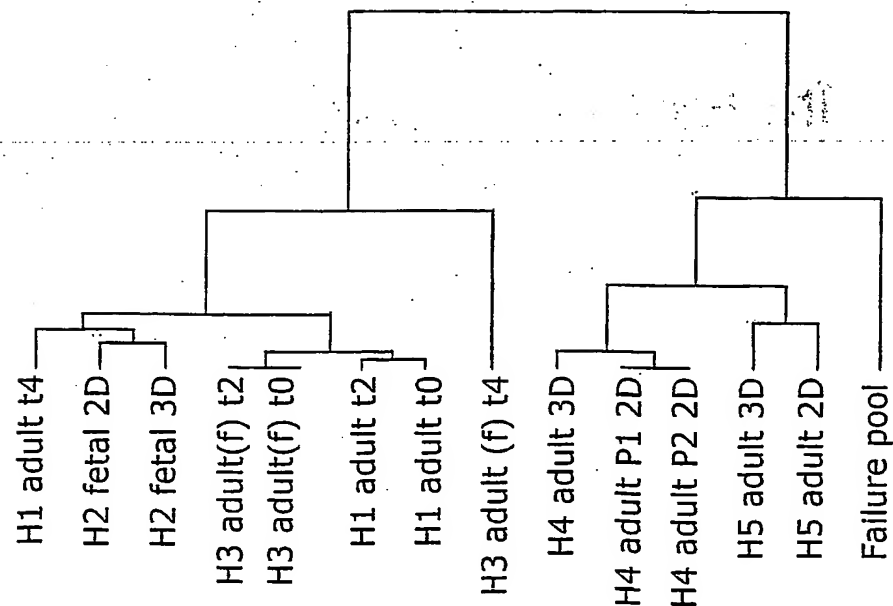
29. Use of a cartilage array or a kit of anyone of claims 12 to 28 for *in vitro* diagnostic of mammals, in particular humans.

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**Fig 1.**



**Fig 2**



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Fig 3

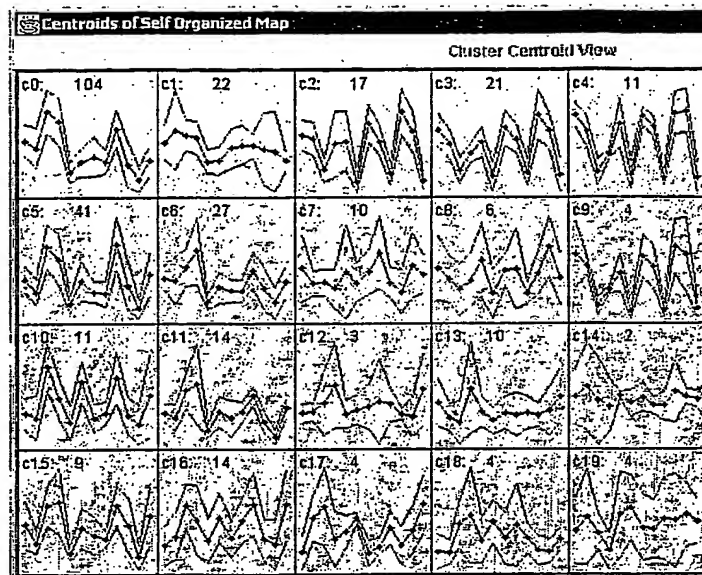
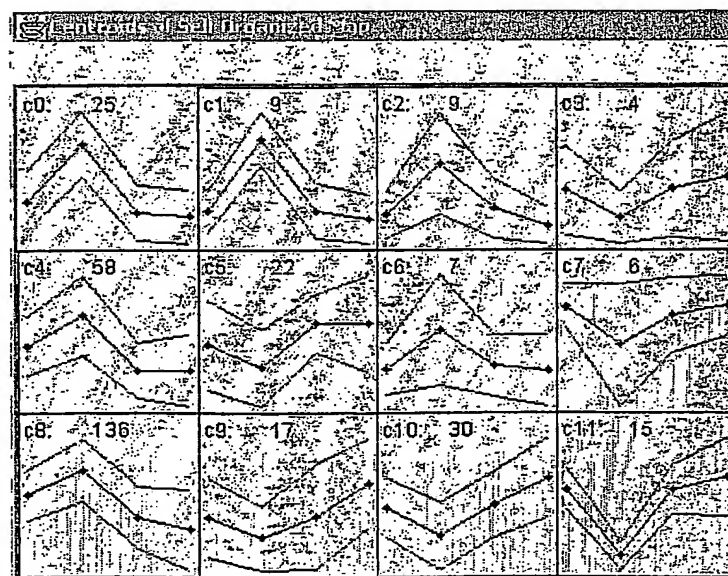


Fig 4



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Fig 5

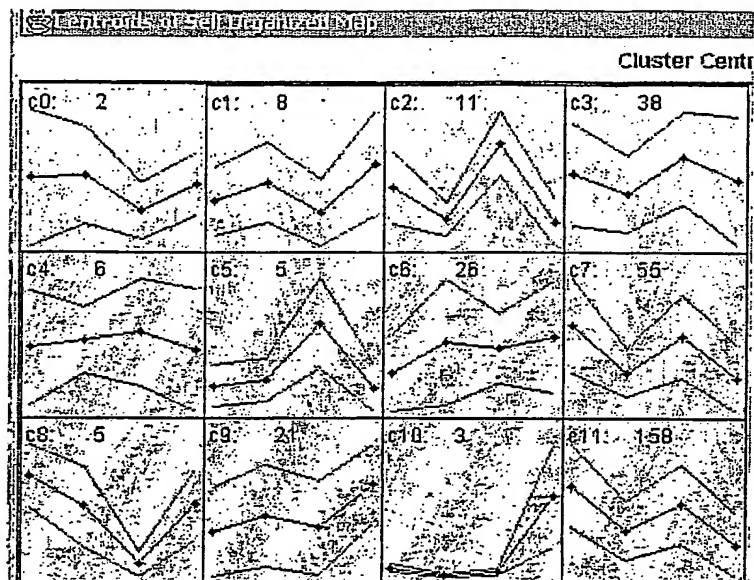
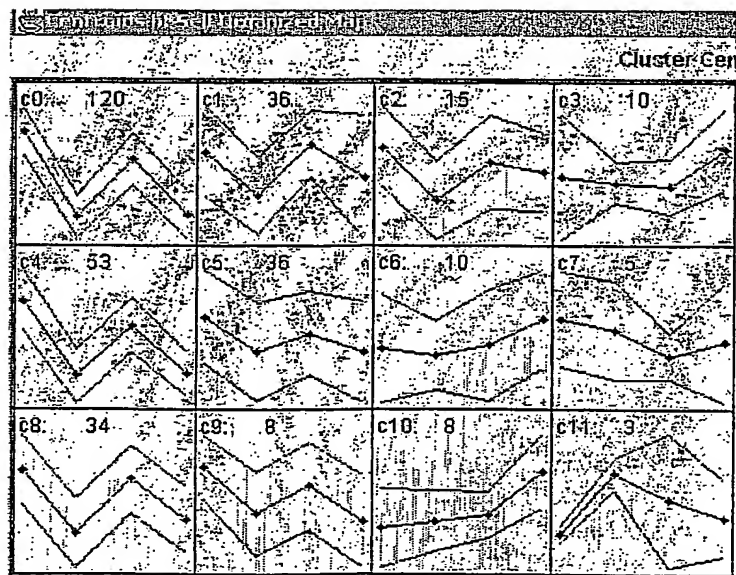


Fig 6



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Fig 7



Homo sapiens mitogen activated protein kinase p38-2 mRNA, complete cds  
 Homo sapiens pancreatic polypeptide PPY, mRNA  
 Homo sapiens frizzled 1 mRNA, complete cds  
 Homo sapiens chondroadherin CHAD, mRNA  
 Human AMP deaminase AMPD3 mRNA, complete cds  
 H.sapiens Pur pur-alpha mRNA, complete cds  
 H.sapiens atk mRNA for agammaglobulinaemia tyrosine kinase  
 Homo sapiens heparan sulfate proteoglycan 2 perlecan HSPG2, mRNA  
 Homo sapiens integrin, beta 4 ITGB4, mRNA  
 Human S-lac lectin L-14-II LGALS2 mRNA, complete cds  
 Homo sapiens troponin I, skeletal, fast TNNI2, mRNA  
 Homo sapiens retinoic acid receptor responder tazarotene induced 2 RARRES2, mRNA  
 H.sapiens mRNA for PHA2I2b protein  
 Homo sapiens glutathione-S-transferase like; glutathione transferase omega GSTTLP28, mRNA  
 Homo sapiens biglycan BGN, mRNA  
 Homo sapiens mRNA for chondromodulin-I precursor, complete cds  
 Homo sapiens integrin, beta 2 antigen CD18 p95,  
 Homo sapiens matrix metalloproteinase 2 gelatinase A, 72kD gelatinase  
 Homo sapiens aggrecan 1 chondroitin sulfate proteoglycan 1  
 Homo sapiens creatine transporter mRNA, complete cds  
 Human mRNA for cone-specific cGMP phosphodiesterase gamma subunit, complete cds  
 H.sapiens mRNA for CLPP  
 Homo sapiens integrin binding protein Del-1 Dell mRNA, complete cds  
 Homo sapiens tissue inhibitor of metalloproteinase 1 erythroid potentiating activity  
 Homo sapiens collagen, type II, alpha 1, COL2A1, transcript variant 2, mRNA  
 Homo sapiens transforming growth factor, beta-induced, 68kD TGFBI, mRNA  
 Human mRNA for eukaryotic initiation factor 4A1  
 H.sapiens dermatopontin mRNA, complete CDS  
 Homo sapiens matrix metalloproteinase 7 matrilysin, uterine MMP7, mRNA  
 Human alpha-1 type XI collagen COL11A1 mRNA, complete cds  
 Homo sapiens cytochrome c oxidase subunit VIIc COX7C, mRNA  
 Alpha tubulin  
 Homo sapiens transketolase Wernicke-Korsakoff syndrome TKT, mRNA  
 beta actin  
 Homo sapiens insulin-like growth factor 1 somatomedin C IGF1, mRNA  
 Human parathyroid hormone-related protein mRNA, complete cds  
 Homo sapiens chloride channel 7 CLCN7, mRNA  
 Homo sapiens RING zinc finger protein RZF mRNA, complete cds  
 Homo sapiens osteoclast stimulating factor mRNA, complete cds  
 Human B-cell leukemia/lymphoma 2 bcl-2 proto-oncogene mRNA encoding bcl-2-alpha protein  
 Human zinc-finger protein C2H2-150 mRNA, complete cds  
 Arabidopsis control oligo  
 Human focal adhesion kinase FAK mRNA, complete cds  
 Homo sapiens calpain 1, mu/I large subunit CAPN1, mRNA  
 Homo sapiens S-adenosylmethionine decarboxylase 1 AMD1, mRNA  
 Human frataxin FRDA mRNA, complete cds  
 Human cleavage and polyadenylation specificity factor mRNA, complete cds  
 H.sapiens COL10A1 gene for collagen alpha-1 type X  
 Homo sapiens G1 to S phase transition 1 GSPT1, mRNA  
 Homo sapiens matrix metalloproteinase 8 neutrophil collagenase MMP8, mRNA  
 Homo sapiens interleukin 3 colony-stimulating factor, multiple IL3, mRNA  
 Human cytochrome bc-1 complex core protein II mRNA, complete cds  
 Human ERK1 mRNA for protein serine/threonine kinase  
 Homo sapiens type 3 iodothyronine deiodinase mRNA, complete cds  
 Homo sapiens GTP-binding protein RHOG, mRNA  
 Human TATA-binding protein associated factor 30 kDa subunit tafII30 mRNA, complete cds  
 Homo sapiens integrin, beta 1 fibronectin receptor, beta polypeptide  
 Homo sapiens caspase 3, apoptosis-related cysteine protease CASP3, mRNA  
 Homo sapiens CD36 antigen collagen type I receptor  
 Homo sapiens integrin, alpha M complement component receptor 3, alpha  
 Human chromatin assembly factor-I p60 subunit mRNA, complete cds  
 Homo sapiens calponin 3, acidic CNN3, mRNA  
 Homo sapiens hypoxanthine phosphoribosyltransferase 1 Lesch-Nyhan syndrome HPRT1, mRNA  
 Human matrix GII protein MGP mRNA, complete cds  
 Human connective tissue growth factor, complete cds  
 glyceraldehyde-3-phosphate dehydrogenase GAPDH mRNA  
 Human helix-loop-helix basic phosphoprotein G0S8 mRNA, complete cds  
 Homo sapiens fibrillin 1 Marfan syndrome FBN1, mRNA  
 Homo sapiens visinin-like 1 VSNL1,  
 Homo sapiens peptidylprolyl isomerase D cyclophilin D PPID, mRNA  
 Homo sapiens lysosomal hyaluronidase LUCA2/HYAL2 mRNA, complete cds  
 Homo sapiens MUF1 protein MUF1, mRNA  
 Homo sapiens glypican 1 GPC1, mRNA  
 Human somatostatin I gene and flanks  
 Homo sapiens integral membrane protein 2A ITM2A, mRNA  
 Homo sapiens group IIE secretory phospholipase A2 mRNA, complete cds  
 Homo sapiens small inducible cytokine A5 RANTES SCYAS, mRNA  
 Homo sapiens aggrecanase-2, ADAMTS5, mRNA  
 Human p21-activated protein kinase Pak1 gene, complete cds  
 Human insulin-like growth factor binding protein 6 IGFBP6 mRNA, complete cds  
 Homo sapiens ribosomal protein L30 mRNA, complete cds  
 Homo sapiens leukemia inhibitory factor cholinergic differentiation factor LIF, mRNA  
 Homo sapiens collagen, type VI, alpha 1 COL6A1, mRNA  
 Homo sapiens collagen, type XVIII, alpha 1 COL18A1, mRNA  
 Human phospholamban chloride channel mRNA, complete cds  
 Homo sapiens growth-arrest-specific protein gas mRNA, complete cds  
 Homo sapiens creatine kinase B mRNA, complete cds  
 Human mRNA for alpha1(X) collagen long form

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Fig 8

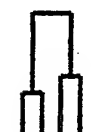


Donor 3 t1d4  
Donor 1 t1d4  
Aortic Fibroblasts  
Donor 4 t1d4  
Donor 2 t1d4

Human matrix Gla protein MGP mRNA, complete cds  
Human helix-loop-helix basic phosphoprotein G0S8 mRNA, complete cds  
Homo sapiens ribosomal protein L18 RPL18 mRNA, complete cds  
Human vimentin gene, complete cds  
Homo sapiens lumican LUM, mRNA  
Human c-jun proto oncogene JUN, complete cds, clone hCJ-1  
Homo sapiens mitochondrial coxII mRNA for cytochrome C oxidase II subunit  
Human ribosomal protein S9 mRNA, complete cds  
Homo sapiens mRNA for chondromodulin-I precursor, complete cds  
Homo sapiens growth-arrest-specific protein gas mRNA, complete cds  
Homo sapiens protein kinase C, beta 1 PRKCB1, mRNA  
Homo sapiens platelet factor 4 PF4, mRNA  
Human fibroblast growth factor-5 FGF-5 mRNA, complete cds  
Human mitochondrial 1,25-dihydroxyvitamin D3 24-hydroxylase mRNA, complete cds  
Homo sapiens integrin, beta 2 antigen CD18 p95, lymphocyte function-associated antigen 1  
Homo sapiens integrin, alpha 2 CD49B, alpha 2 subunit of VLA-2 receptor ITGA2, mRNA  
Human B-cell leukemia/lymphoma 2 bcl-2 proto-oncogene mRNA encoding bcl-2-alpha protein, complete cds  
Human plectin PLECL mRNA, complete cds  
Human focal adhesion kinase FAK mRNA, complete cds  
Human gene for tumor necrosis factor TNF-alpha  
Homo sapiens homeodomain protein BAPX1 mRNA, complete cds  
Human parathyroid hormone-related protein mRNA, complete cds  
Homo sapiens visinin-like 1 VSNL1, mRNA  
Homo sapiens testis-specific Basic Protein Y 1 BFY1 mRNA, complete cds  
Homo sapiens vascular cell adhesion molecule 1 VCAM1, transcript variant 2, mRNA  
Homo sapiens a disintegrin-like and metalloprotease; aggrecanase-2 ADAMTSS, mRNA  
Human Tat-SF1 mRNA, complete cds  
Homo sapiens catechol-O-methyltransferase COMT mRNA, complete cds  
Homo sapiens tensin TNS, mRNA  
Homo sapiens heat shock 70kD protein 1B HSPA1B, mRNA  
Homo sapiens MUF1 protein MUF1, mRNA  
Homo sapiens mRNA for DNA-binding protein, complete cds  
Human ADP/ATP translocase mRNA, 3' end, clone pHAT8  
Homo sapiens collagen, type I, alpha 2 COL1A2, mRNA  
Human mRNA for pro-alpha-1 type 3 collagen  
Homo sapiens collagen, type XVIII, alpha 1 COL18A1, mRNA  
Human phospholemman chloride channel mRNA, complete cds  
Human checkpoint suppressor 1 mRNA, complete cds  
Homo sapiens mRNA for protein phosphatase 2C gamma  
Human hnRNP H mRNA, complete cds  
Homo sapiens integrin, alpha L antigen CD11A p180  
Homo sapiens frizzled 1 mRNA, complete cds  
Human mRNA for alpha1(X) collagen long form  
Homo sapiens ribosomal protein L13 RPL13, transcript variant 1, mRNA  
Homo sapiens eukaryotic translation initiation factor 5 EIF5, mRNA  
Homo sapiens caspase 3, apoptosis-related cysteine protease CASP3, mRNA  
Homo sapiens interleukin 6 interferon, beta 2 IL6, mRNA  
Homo sapiens interleukin 8 IL8, mRNA  
Homo sapiens decay accelerating factor for complement CD55, Cromer blood group system DAF, mRNA  
Homo sapiens similar to chondroitin sulfate proteoglycan 2 versican H. sapiens LOC153633, mRNA  
Homo sapiens eIF-2-associated p67 homolog mRNA, complete cds  
Homo sapiens troponin I, skeletal, fast TNNT2, mRNA  
Human p37NB mRNA, complete cds  
Homo sapiens creatine kinase B mRNA, complete cds  
H. sapiens P1-Cdc46 mRNA  
Human Smad1 mRNA, complete cds  
Homo sapiens integrin, beta 1 fibronectin receptor, beta polypeptide, antigen CD29 includes MDP2  
Human cytoskeleton associated protein CG22 mRNA, complete cds  
Alpha tubulin  
Homo sapiens matrix metalloproteinase 1 interstitial collagenase MMP1, mRNA  
Homo sapiens chloride channel 7 CLCN7, mRNA  
Homo sapiens RING zinc finger protein RZF mRNA, complete cds  
Human pancreatic elastase IIA mRNA, complete cds  
Homo sapiens regulator of G-protein signalling 4 RGS4, mRNA  
Human L2-9 transcript of unrearranged immunoglobulin VH5 pseudogene  
Human HLA-DMB mRNA, complete cds  
Human putative tumor suppressor LUCA15 mRNA, complete cds  
H. sapiens mRNA for VEGF-C protein  
Human profilin mRNA, complete cds  
Homo sapiens matrix metalloproteinase 3 stromelysin 1, progelatinase MMP3 gene, complete cds  
Homo sapiens transforming growth factor, beta-induced, 68kD TGFBI, mRNA  
Homo sapiens tissue inhibitor of metalloproteinase 1 erythroid potentiating activity, TIMP1, mRNA

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Fig 9



P3 3D IL-1 10h  
P3 3D IL-1 7d  
P3 3D 16h  
P3 3D 7d

Homo sapiens integral membrane protein 2A ITM2A, mRNA  
Homo sapiens small inducible cytokine A5 RANTES SCYA5, mRNA  
Human ERK1 mRNA for protein serine/threonine kinase  
Homo sapiens fibromodulin FMOD, mRNA  
Homo sapiens collagen alpha 3 type IX COL9A3 mRNA, complete cds  
H.sapiens dermatopontin mRNA, complete CDS  
H.sapiens mRNA for leucine zipper protein  
Homo sapiens fibronectin 1 FN1, mRNA  
glyceraldehyde-3-phosphate dehydrogenase GAPDH mRNA, complete cds  
Human mRNA for pro-alpha-1 type 3 collagen  
phospholipase A2  
Human alpha-1 type XI collagen COL11A1 mRNA, complete cds  
Homo sapiens collagen, type II, alpha 1 primary osteoarthritis, spondyloepiphyseal dysplasia  
Homo sapiens ATPase, Cu++ transporting, beta polypeptide Wilson disease ATP7B, mRNA  
Homo sapiens homolog of the Aspergillus nidulans sudD gene product mRNA, complete cds  
Homo sapiens cadherin 11, type 2, OB-cadherin osteoblast CDH11, transcript variant 1, mRNA  
Homo sapiens cathepsin B CTSB, mRNA  
Homo sapiens decorin DCN, mRNA  
Homo sapiens SRY sex determining region Y-box 9 campomelic dysplasia  
Human ribosomal protein S9 mRNA, complete cds  
Homo sapiens nuclear autoantigenic sperm protein histone-binding NASP, mRNA  
H.sapiens mRNA for Sop2p-like protein  
Homo sapiens calpain 1, mu/I large subunit CAPN1, mRNA  
Homo sapiens defender against cell death 1 DAD1, mRNA  
Homo sapiens caspase 9, apoptosis-related cysteine protease CASP9, transcript variant alpha, mRNA  
Human AMP deaminase AMPD3 mRNA, complete cds  
Homo sapiens mRNA for leukemia associated gene 1  
Homo sapiens pancreatic polypeptide PPY, mRNA  
Homo sapiens msh homeo box homolog 2 Drosophila MSX2, mRNA  
Homo sapiens creatine transporter mRNA, complete cds  
Human cytoskeleton associated protein CG22 mRNA, complete cds  
Homo sapiens collagen, type I, alpha 1 COL1A1, mRNA  
Homo sapiens S-adenosylmethionine decarboxylase 1 AMD1, mRNA  
H.sapiens mRNA for RIT protein  
H.sapiens Pur pur-alpha mRNA, complete cds  
Homo sapiens talin 1 TLN1, mRNA  
Homo sapiens phosphatase and tensin homolog mutated in multiple advanced cancers 1 PTEN, mRNA  
Homo sapiens peptidylprolyl isomerase D cyclophilin D PPID, mRNA  
Homo sapiens matrix metalloproteinase 7 matrilysin, uterine MMP7, mRNA  
Homo sapiens phosphoenolpyruvate carboxykinase 1 soluble PCK1, mRNA mRNA carboxykinase 1 soluble  
Homo sapiens RING zinc finger protein RZF mRNA, complete cds  
Homo sapiens RPL6 gene for ribosomal protein L6, complete cds  
Homo sapiens cartilage oligomeric matrix protein pseudoachondroplasia, epiphyseal dysplasia 1  
Homo sapiens ribosomal protein L18 RPL18 mRNA, complete cds  
Homo sapiens hexabrachion tenascin C, cytactin HXB, mRNA  
Homo sapiens biglycan BGN, mRNA  
Homo sapiens bone morphogenetic protein 6 BMP6, mRNA  
Homo sapiens osteoclast stimulating factor mRNA, complete cds  
Homo sapiens collagen, type I, alpha 2 COL1A2, mRNA  
Human tropomodulin mRNA, complete cds  
Human insulin-like growth factor binding protein 5 IGFBP-5 mRNA, complete cds  
Homo sapiens bone morphogenetic protein 9 BMP9 mRNA, complete cds  
Homo sapiens ATP synthase, H+ transporting, mitochondrial F1 complex, delta subunit ATP5D, mRNA  
Homo sapiens interleukin 6 interferon, beta 2 IL6, mRNA  
Homo sapiens cyclin D1 PRAD1: parathyroid adenomatosis 1 CCND1, mRNA  
Homo sapiens platelet factor 4 PF4, mRNA  
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Homo sapiens tissue inhibitor of metalloproteinase 1 erythroid potentiating activity, TIMP1  
Human tax1-binding protein TXBP181 mRNA, complete cds  
Homo sapiens lipase A, lysosomal acid, cholesterol esterase Wolman disease LIPA, mRNA  
Homo sapiens transketolase Wernicke-Korsakoff syndrome TKT, mRNA  
Homo sapiens matrilin 1, cartilage matrix protein MATN1, mRNA  
Homo sapiens GTP-binding protein RHOG, mRNA  
Homo sapiens leukemia inhibitory factor cholinergic differentiation factor LIF, mRNA  
Homo sapiens vascular cell adhesion molecule 1 VCAM1, transcript variant 2, mRNA  
Homo sapiens growth-arrest-specific protein gas mRNA, complete cds  
Homo sapiens mitogen activated protein kinase p38-2 mRNA, complete cds  
Human transcription factor IL-4 Stat mRNA, complete cds  
Human insulin-like growth factor binding protein 6 IGFBP6 mRNA, complete cds  
Homo sapiens FOS-like antigen 1 FOSL1, mRNA  
Homo sapiens integrin, beta 4 ITGB4, mRNA  
Human putative tRNA synthetase-like protein mRNA, complete cds  
Human mRNA for retinol binding protein RBP  
Homo sapiens tissue inhibitor of metalloproteinase 2 TIMP2, mRNA  
Homo sapiens collagen, type V, alpha 1 COL5A1, mRNA

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ning of each regular issue of the PCT Gazette.*

(54) Title: IDENTIFICATION OF SPECIFIC MARKER GENES AND USE THEREOF

(57) Abstract: A cartilage array comprises a plurality of different polynucleotide probe spots stably associated with a solid surface of a carrier, whereby each of said spots is made of a unique polynucleotide that corresponds to one specific cartilage marker gene. Said specific cartilage marker genes preferably are at least in part selected from a group of 467 genes that could be shown to be cartilage related.

WO 2003/106706 A3

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# INTERNATIONAL SEARCH REPORT

International Application No.

PCT/CH 03/00379

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BENZ ET AL.: "Molecular analysis of expansion, differentiation, and growth factor treatment of human chondrocytes identifies differentiation markers and growth-related genes"</p> <p>BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 293, no. 1, 26 April 2002 (2002-04-26), pages 284-292, XP002256352 the whole document</p> <p style="text-align: center;">----- -/--</p>	1-12

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

### ° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

7 October 2003

Date of mailing of the international search report

16. 01. 2004

Name and mailing address of the ISA

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Bort, S

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## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/CH 03/00379

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	STOKES ET AL.: "Assessment of the gene expression profile of differentiated and dedifferentiated human fetal chondrocytes by microarray analysis" ARTHRITIS AND RHEUMATISM, vol. 46, no. 2, February 2002 (2002-02), pages 404-419, XP002253145 the whole document -----	1-12
X	SCHNABEL ET AL.: "Dedifferentiation-associated changes in morphology and gene expression in primary human articular chondrocytes in cell culture" OSTEOARTHRITIS AND CARTILAGE, vol. 10, no. 1, January 2002 (2002-01), pages 62-70, XP002253146 the whole document -----	1-12
X	MARLOVITS ET AL.: "Differential gene-expression of human articular chondrocytes and human fibroblasts in two- and three-dimensional cell culture" FASEB JOURNAL, vol. 15, no. 4, 7 March 2001 (2001-03-07), page A34, XP008021552 the whole document -----	1-12
X	ISLAM ET AL.: "Expression profile of protein tyrosine kinase genes in human osteoarthritis chondrocytes" OSTEOARTHRITIS AND CARTILAGE, vol. 9, 2001, pages 684-693, XP002253148 the whole document -----	1-12
A	KURELLA ET AL.: "DNA microarray analysis of complex biologic processes" J AM SOC NEPHROL, vol. 12, 2001, pages 1072-1078, XP002253149 the whole document -----	

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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CH 03/00379

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
~~because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).~~

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-12

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-12

Invention 1

A method for the identification of tissue/cell specific marker genes; a method for the determination of a particular disease state or developmental status or the physiological potential of cell/tissue; and a method for the determination of characteristic gene expression profiles for clinical use

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2. claims: 13-29 (all partially)

Inventions 2-468

An array comprising a human chondrocyte specific gene; a kit comprising it; and the use of said gene or kit for in vitro diagnostic of mammals, in particular humans,

wherein said human chondrocyte specific gene is that corresponding to the Pubmed accession numbers listed in table II:

-for invention 2: AA283693

-for invention 3: AA845156

-for inventions 4-468: R52548-AA504477

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